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DEVELOPMENT OF DUTASTERIDE LOADED MOUTH DISSOLVING TABLET AND USING DIRECT COMPRESSION METHOD

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ABSTRACT

This study aimed to create dutasteride mouth dissolve tablets using the direct compression technique and superdisintegrant addition. Superdisintegrant addition technique was chosen for future research because it had the lowest disintegration time out of the nine formulations when hardness and friability were taken into consideration. Nine further batches (F1-F9) were produced utilizing SSG, crospovidone, and croscarmellose sodium in varying quantities. Weight variation, hardness, friability, drug content, and the best formulation for mouth-dispersing tablets were all assessed for each formulation. The pure dosage calibration curve was generated by dissolving the drug into ethanol & measuring its absorbance with a UV spectrophotometer calibrated to 241.5 nm. The R2 score was 0.999.The size of dutasteride particle predictions was done using light microscopy. The particles were 2.1 µm in size. All the prepared formulations were undergone for their characterization. The optimized formulation showed that 99% of the medicament was released in 4 minutes. However, its wetting time and disintegration time are 26 and 30 sec, respectively.

KEYWORDS: *Crospovidone, Croscarmellose Sodium, Sodium Starch Glycolate, Ethanol, Dutasteride*

INTRODUCTION

Despite the inherent drawback, oral medication administration is still a common method of drug delivery. Solid dose forms are preferred over parenteral because they are simple to administer, allow for self-medication, and help patients avoid discomfort. One such strategy is the development of mouth dissolving or mouth integrating tablets, which, according to the action of superdisintegrants inside the formulation, dissolve quickly in saliva without the need for water within a matter of seconds.[1]

The primary advantage of the mouth dissolving dosage form is that they are doing not have to be chewed because they disintegrates quickly and completely within the bit of saliva within the mouth. Superdisintegrants, which offer instantaneous tablet disintegration after placing it on the tongue and releasing the medication in saliva, are the fundamental strategy used in the development of mouth-dissolving tablets. Some medications are more bioavailable due to oral absorption in the mouth as well as pregastric absorption of saliva that contains dispersed medications and passes into the stomach.In contrast to simple tablets, more critically, fewer medicines are prone to first pass metabolism.[2]

Hair loss and benign prostatic hyperplasia (BPH) are both conditions treated with dutasteride. It is a type I and type II 5-reductase competitive inhibitor. Studies show that dutasteride can increase the weight of developing ovarian and testicular tissue while reducing the weight of developing adrenal and prostate tissue. Due to the FDA's

classification of it as pregnancy category X,Pregnant or potentially pregnant women should not use or handle dutasteride.[3, 4]

Dutasteride is exclusively sold as soft gelatin capsules and is classified as Bio pharmaceutics classification System (BCS) class II due to its restricted water solubility. Due to the ease with which dutasteride is absorbed via the skin; these concerns might result in a wide range of health problems.Dutasteride must thus be created in a mouth-dispersing tablet form in order to improve its safety and bioavailability. Additionally, a smaller solid tablet is anticipated to increase patient compliance. Additionally, since tamsulosin and dutasteride are frequently administered together for BPH,solid dosage formulations might be more useful for fixed dose combos with other drugs.[5, 6]

Mouth Dissolving Phenomenon

Superdisintegrants are given far greater consideration when creating mouth-dispersing pills. By inducing swelling and water absorption in the pill, they offer quick disintegration. The swelling mechanism of the superdisintegrants wets the carrier & surface, which enhances tablet disintegration and causes increased dissolution to occur.[7]

The swelling capacity in the dissolving liquid and matrix density both affect how well superdisintegrants act. A greater degree of disintegration is caused by a matrix with a higher swelling capacity and density.

MATERIAL AND METHODS

Material

Dutasteride was purchased from yarrow camp (India). Microcrystalline cellulose, mannitol, sodium starch glycolate, croscarmelose, aerosil, and aspartame all these ingredients came from Central drug house, New Delhi.

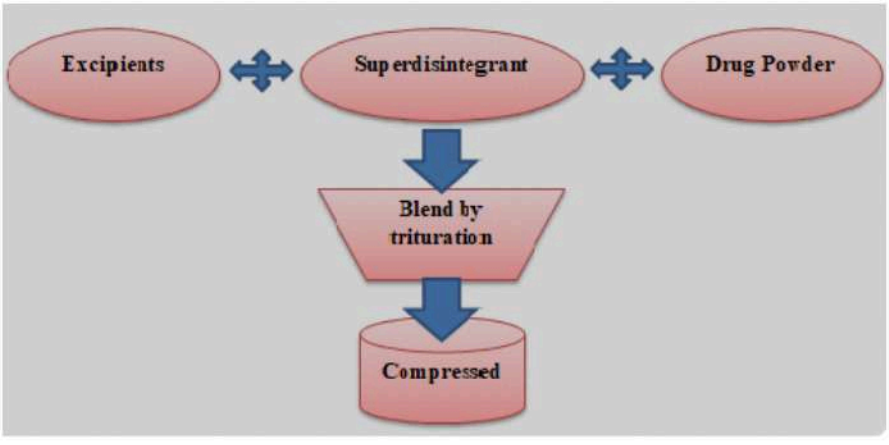
Method

Direct Compression Method

It is a method that allows tablets to be crushed straight from medication and excipient mixes, without any prior processing. It delivers excellent efficiency and has advantages over other tablet production methods like wet granulation. The mixture that is to be compressed needs to flow properly and cohere under pressure. The method by which mouth-dissolving pills disintegrate and dissolve heavily relies on superdisintegrants. A high disintegration rate must be ensured by selecting the right kind and quantity of disintegrants. Other formulation elements like effervescent agents or water-soluble excipients can be added to improve the dissolution or disintegration qualities even more. The disintegrant addition technology is the most popular method for making tablets because it has a number of benefits, including the ability to accommodate high doses, cost effectiveness, the simplest method for making tablets, and the use of conventional equipment and excipients that are widely accessible. Small, very soft tablets have minimal mechanical strength, while hard, massive tablets display longer disintegration times. Use the optimal type and concentration of disintegrant to produce rapid disintegration and high dissolving rates.[8]

MCC plastically deforms upon compression, maximising the area of interparticle connection. Numerous hydrogen bonds can form due to the close proximity of hydrogen groups on nearby cellulose molecules, and these connections are virtually entirely responsible for the cohesiveness and strength of compacts, even when compression pressures are moderate. It has also been proposed that elongated and unevenly shaped MCC particles mechanically interlock to improve tabletability.[9]

Figure 1: Showing Direct Compression Technique



Preparation of Dutasteride Mouth Dissolving Tablets

Before being mixed, all necessary excipients were filtered through an 80 mesh screen. All additional excipients, including dutasteride, were physically combined in a mortar for ten minutes. The sweetener is responsible for the mixture's appealing flavour. The powder mixture was then compressed into tablets using a flat face, 9-mm diameter rotary tablet punching machine. There are different formulation batches with different excipients concentrations as given in Table 1.

RESULTS AND DISCUSSION

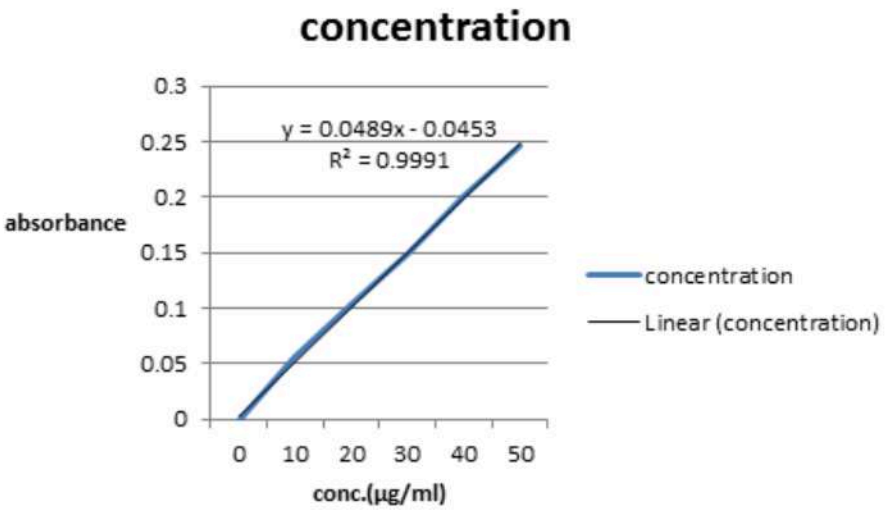
Calibration Curve of Dutasteride

Dutasteride, the stock solution, was carefully weighed out at 100 mg and diluted in 100 ml of 0.1 N HCL in a 100 ml volumetric flask to construct a calibration curve. To make the concentrations of 10 to 50 g/ml, 2, 4, 6,... ml of the stock solution were pipette out and raised to 10 ml with 0.1 N HCL as shown in figure1. Using a spectrophotometer (schimazdu, uv-1700, Japan), the produced concentrations were examined at 271.5 nm. Calibration curve of dutasteride as given in Figure 1.

Table 1: Different Formulation Batches With Different Excipients Concentration

Name of Ingredients	Quantity(mg)								
	f1	f2	f3	f4	f5	f6	f7	f8	F9
Dutasteride	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
MCC	40	38	36	40	38	36	40	38	36
Mannitol	21	21	21	21	21	21	21	21	21
Sod. Starch glycolate	12	14	16	-	-	-	-	-	-
Crosscarmilose sodium	-	-	-	12	14	16	-	-	-
crospovidone	-	-	-	-	-	-	12	14	16
Aerosil	2	2	2	2	2	2	2	2	2
Aspartame	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Total	80	80	80	80	80	80	80	80	80

Figure 2: Showing Calibration Curve



Drug Identification Through Infrared Spectroscopy

For this purpose, the infrared spectrum of dutasteride was determined and was matched with the standard monograph given in Indian Pharmacopoeia as shown in Figures 3 and 4.

The above Table represents the results of prepared formulations (f1 to f9) as wetting time, disintegration time and hardness of the dutasteride mouth dissolving tablets.

EVALUATION OF PREPARED DUTASTERIDE MOUTH DISSOLVING TABLETS

Weight-variation

Twenty tablets were randomly selected from each formulation and tested using a Shimadzu digital balance (Type-AUY 220, No.-D449811085). The weight distribution was then calculated. The weight of each tablet was then calculated and contrasted with an average weight. A digital screw gauge micrometre was used to measure the thickness of ten tablets at random from each formulation.[10]

Thickness

A digital screw gauge micrometre was used to measure the thickness of ten tablets at random from each formulation as shown in Table 3 and Figure 5.

Hardness and Friability

The testing device for tablet hardness allowed evaluation of the researched orally disintegrating tablet formulations'

Figure 3: IR Spectrum of Dutasteride

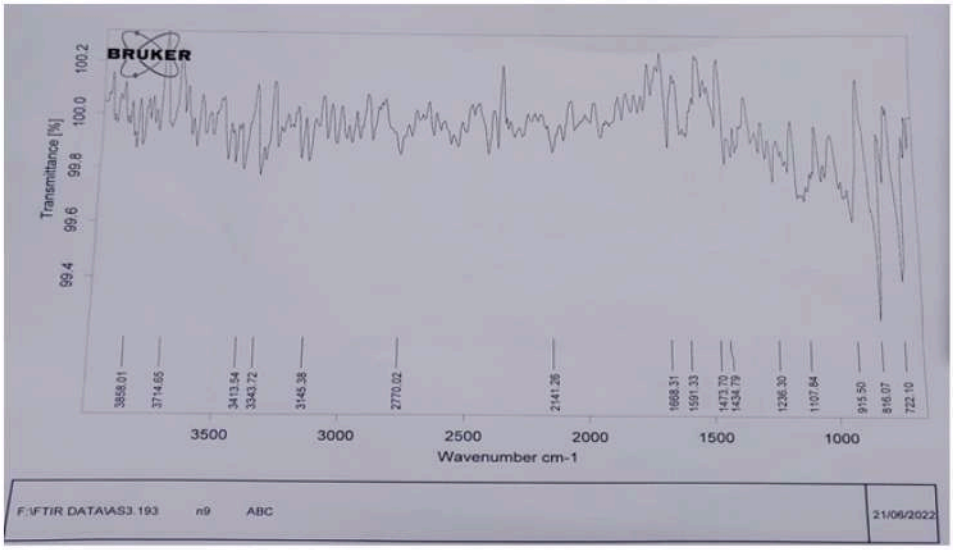


Figure 4: IR Spectrum of Excipients

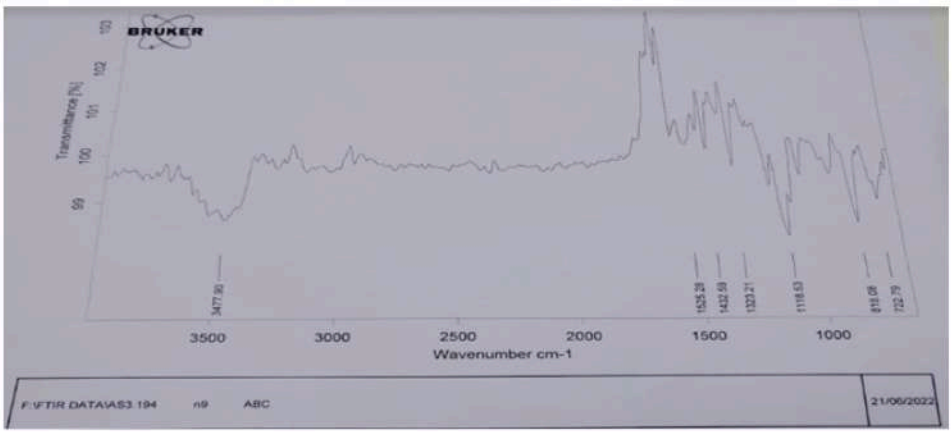


Table 2: Formulation Development and Optimization			
Formulations (F)	**Wetting time (sec)**	**Disintegration time (sec)**	**Hardness (kg/cm²)**
F1	51	55.24	3
F2	59	65.21	3
F3	48	45.11	3
F4	31	35.33	1.6
F5	29	32.53	1.6
F6	26	30.30	3
F7	41	43.27	1.5
F8	36	46.11	2.2
F9	34	44.39	2.1

Table 3: Thickness of Tablet of Prepared Batches	
Formulations (F)	**Thickness(mm)**
f1	2.2
f2	2.2
f3	2.3
f4	2.2
f5	2.2
f6	2.2
f7	2.3
f8	2.3
f9	2.2

crushing strength (Monsanto type). A sample of 20 orally disintegrating tablets was evaluated for friability using a USP-type Roche friabilator (Camp-bell Electronics, Mumbai).[11] The preweighed tablets were placed in a plastic chambered friabilator that was attached to a motor evolving at a speed of 25 rpm for 4 minutes. After the tablets had been dedusted and reweighed, their % weight loss (friability) was calculated as shown in Table 4 and Figure 6. [12]

% Friability = [(Initial weight- Final weight) / (initial weight)] x 100

Wetting Time

The wetting time of the oral dissolving tablet is another important factor to investigate since it sheds light on capillarity and, consequently, the tablet's integration capabilities. The dosage form's wetting time is determined by the contact angle. The pill will deteriorate more quickly with a shorter wetting time. The proposed method was used to determine the wetting time. The tissue paper was folded twice and put in a tiny petri dish with 6 ml of room temperature water. The tablet was placed on the tissue paper and left to soak up the liquid fully. After then, it was noted in the second portion of the table how long it took to thoroughly wet the pill.[13] as shown in Table 5 and Figure 7.

Figure 4: Thickness of the Prepared Batches

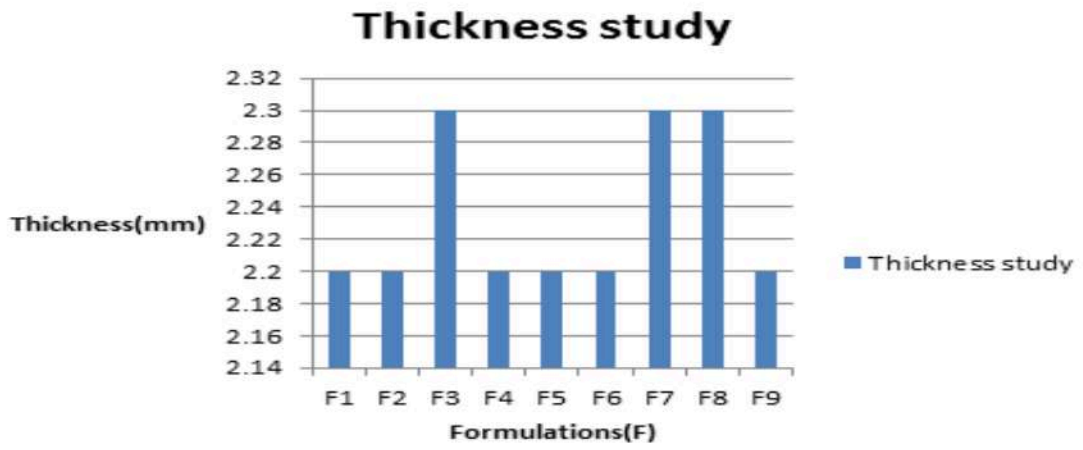


Table 4: Hardness Of Different Batches

Formulations (F)	Hardness (kg/cm²)
F1	3
F2	3
F3	3
F4	1.6
F5	1.6
F6	3
F7	1.5
F8	2.2
F9	2.1

Figure5: Represents The Hardness of Batches

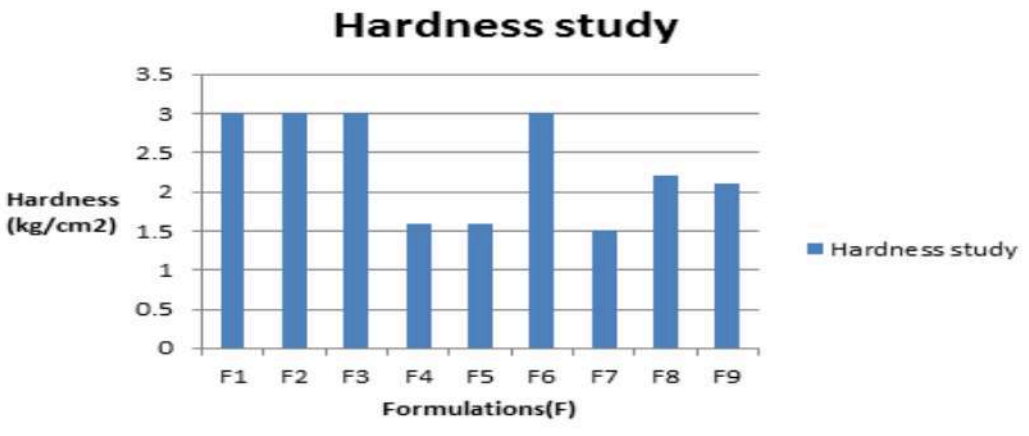
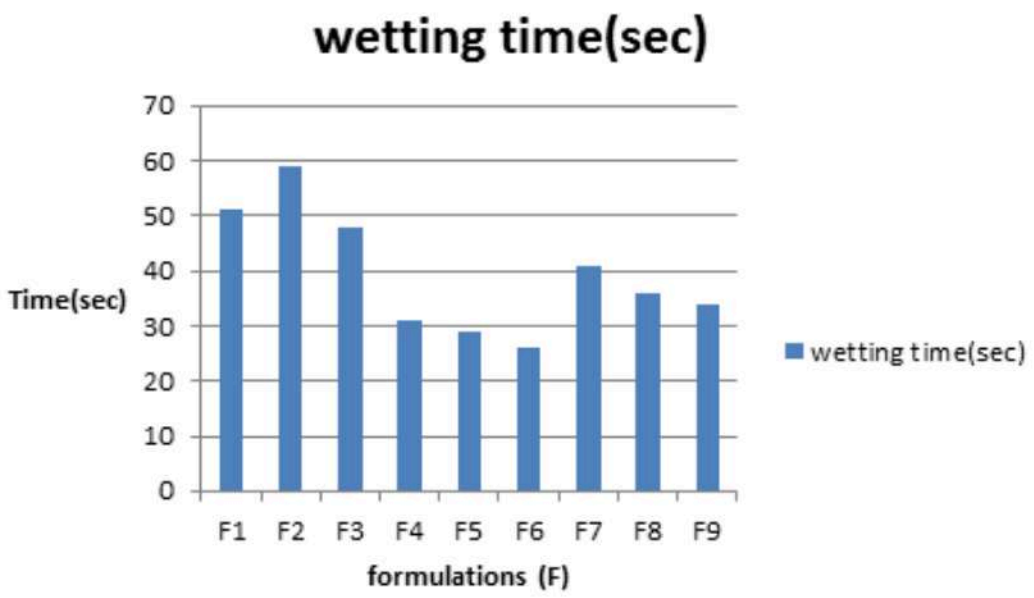


Table 5: Showing Wetting Study	
Formulations	**Wetting time (sec)**
F1	51
F2	59
F3	48
F4	31
F5	29
F6	26
F7	41
F8	36
F9	34

Figure 6: Wetting Time Of The Formulations



Disintegration Time

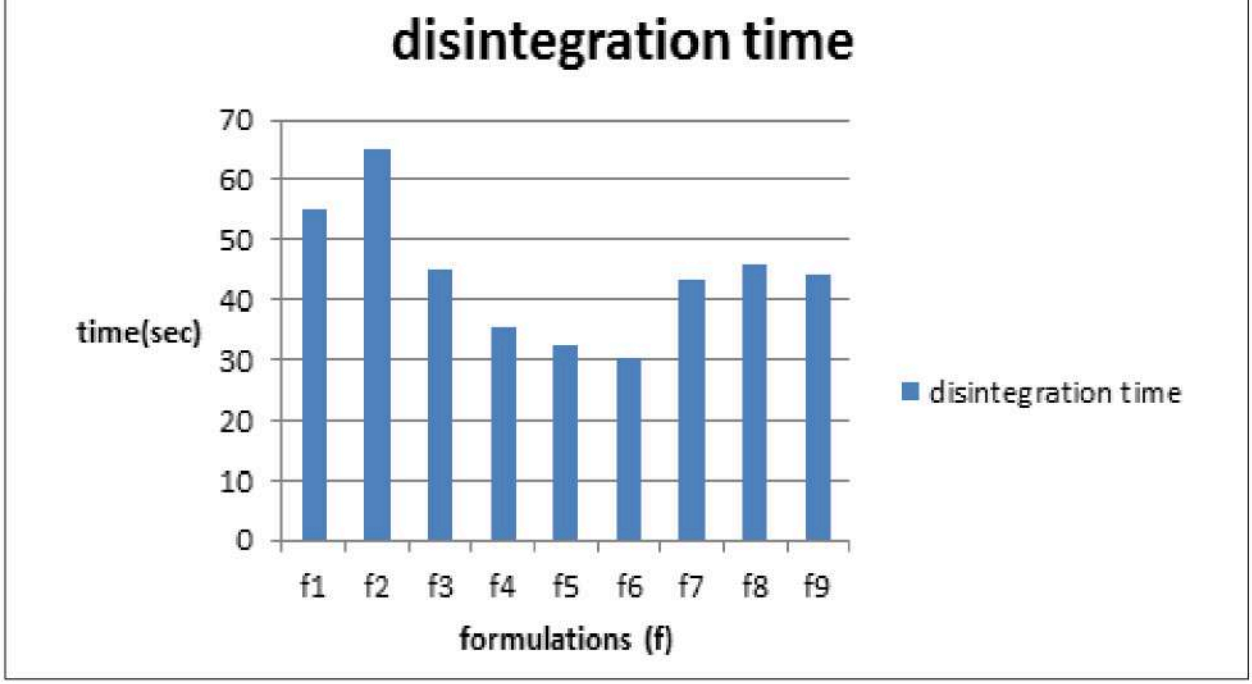
In the experiment, tablets were employed, and the disintegration media was distilled water. [14] The amount of time, measured in seconds, it took for the pills to completely dissolve and leave no bulk inside the instrument was recorded as shown in table 6 and figure 7.

In- vitro Dissolution Test

A process that is very similar to that used to create dissolve methods for traditional tablets is utilised to create dissolve techniques for mouth-dissolving tablets. The USP monograph states that dissolving circumstances may exist with respect to medications. Other media, such as 0.1N HCL, pH 6.8 phosphate buffers, should be utilized for MDT evaluation, much as their pill equivalents. With the USP apparatus II, the dissolution was carried out at 50 rpm and 37 +/- 0.5 °C for the dissolving medium. Large tablets, such as those containing thick particles and weighing more than one gramme, increase paddle speed to stop a quantity in the vessel from dissolving. Now, 25–75 rpm is the ideal range for stirring under these two conditions. Despite the

Table 6: Disintegration Time(Sec)	
Formulations (F)	**Disintegration Time(sec)**
F1	55.24
F2	65.21
F3	45.11
F4	35.33
F5	32.53
F6	30.30
F7	43.27
F8	46.11
F9	44.39

Figure 7: Showing the Disintegration Time Study of the Tablets



appealing MDT uses of the USP 1 (basket) device, Due of the physical characteristics of tablets, it is rarely used. [15]

The formulas F3, F6, and F7 were judged to be the most suited based on several parameters. As a consequence, the dissolving test of these formulations was conducted, with the following results:

The formulas F3, F6, and F7 were judged to be the most suited based on several parameters. As a consequence, these formulations' dissolving test was carried out, and results were obtained. According to the findings, the cumulative drug release from F6 is about 99% in 240 seconds as seen in the table above. This shows that out of the batch of all nine formulations, formulation F6 is the best potential optimised formulation.

Based on the findings (table 7,8,9 & figure 8,9,10), an improved formulation for mouth-dissolving tablets was chosen. F6 chose a drug release study based on the composition of the aforementioned requirements. We

Table 7: Cumulative % Drug Release Of Formulation F6						
S. No.	Time (sec)	Concentration X D.F (mg/ml)	Concentration mg/5ml	Concentration mg/900ml	Percentage Cumulative Drug Release	Percentage Drug Rrelease
1.	0	0	0	0	0	0
2.	30	0.000042	0.00021	0.189	0.189	37.8
3.	60	0.000048	0.00024	0.216	0.220	44
4.	120	0.000068	0.00034	0.306	0.3065	61.3
5.	180	0.000096	0.00048	0.432	0.433	86.6
6.	240	0.00011	0.00055	0.495	0.496	99.2

Figure 8: Cumulative % Drug Release of Formulation 6

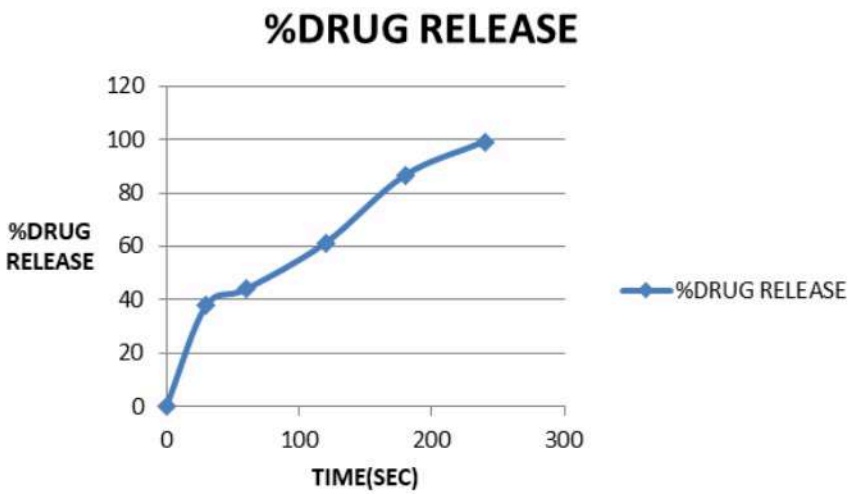


Table 8: Cumulative % Drug Release of Formulation 3						
S. No.	Time (sec)	Concentration X D.F (mg/ml)	Concentration mg/5ml	Concentration mg/900ml	Percentage Cumulative Drug Release	Percentage Drug Rrelease
1.	0	0	0	0	0	0
2.	30	0.000032	0.00016	0.144	0.1440	28.80
3.	60	0.000042	0.00021	0.189	0.1892	37.84
4.	180	0.000054	0.00027	0.243	0.2434	48.68
5.	300	0.000070	0.00035	0.315	0.3160	63.20
6.	420	0.000092	0.00046	0.414	0.4150	83.00
7.	540	0.000108	0.00054	0.486	0.4874	97.48

Figure 9: % Drug Release of Formulation 3

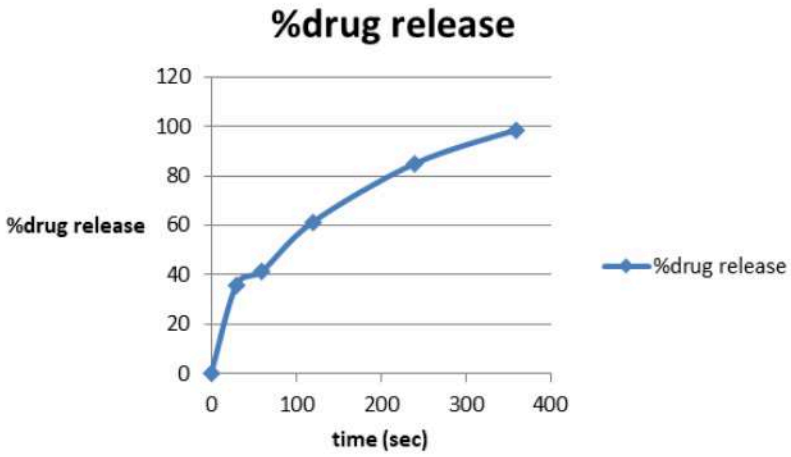
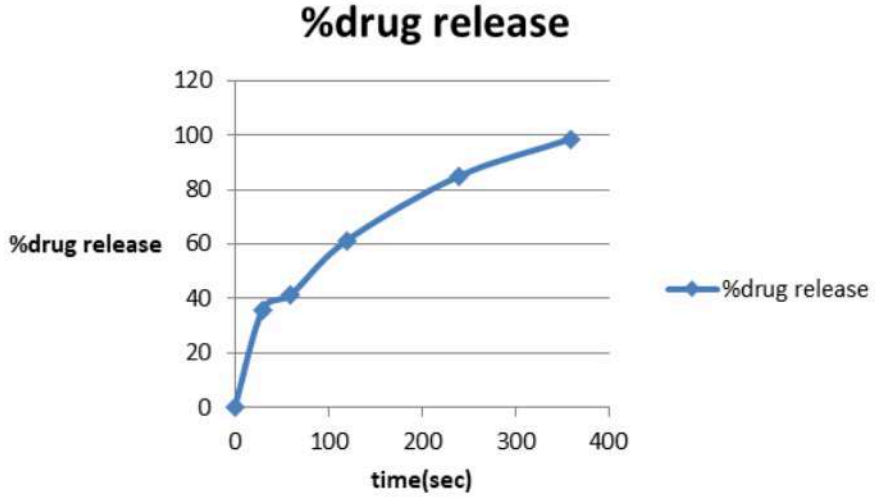


Table 7: Cumulative % Drug Release Of Formulation F7

S. No.	Time (sec)	Concentration X D.F (mg/ml)	Concentration mg/5ml	Concentration mg/900ml	Percentage Cumulative Drug Release	Percentage Drug Rrelease
1.	0	0	0	0	0	0
2.	30	0.000040	0.00020	0.180	0.1800	36.00
3.	60	0.000046	0.00023	0.207	0.2072	41.44
4.	120	0.000068	0.00034	0.306	0.3084	61.28
5.	240	0.000094	0.00047	0.423	0.4240	84.80
6.	360	0.000109	0.000545	0.491	0.4922	98.44

Figure 10: % Drug Release of Formulation 7



investigated in-vitro drug release for 4 minutes. 99% of the medication in formulation f6 diffused in 4 minutes, according to the drug profile's release data. Hence, this study confirms that formulation f6 was an optimized formulation among all mouth dissolving tablet formulations.

CONCLUSION

The goal of this study was accomplished with the effective preparation of the mouth-dissolving dutasteride tablets employing the direct compression technique and superdisintegrants. According to in-vitro disintegration, formulation F6 made with croscarmelose sodium had a quicker disintegration rate than SSG.

This indicates that the release of the medication dutasteride is increased by the use of superdisintegrants. In light of this, it may be said that dutasteride was best delivered via mouth-dissolving tablets.

Therefore, the mouth-dissolving tablets are effectively created for patients who have dysphagia or trouble swallowing, who are primarily senior patients or who do not have access to water, and they also offer faster and better drug release, thereby boosting the bioavailability of the medicine.

With better patient compliance, convenience, bioavailability, and a quick beginning of action, the FDTs have potential advantages over traditional oral dose forms, which has attracted the interest of numerous manufacturers for more than a decade. The FDT formulations made possible by several of these technologies are sufficiently strong mechanically and dissolve quickly in the mouth. Many medications, especially tasteless drugs, can be included in FDT. The investigation is still ongoing. For this technology to be used effectively, more goods must be developed. Because of this, FDT could soon be produced for the majority of medications.

Conflicts of interest: None

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