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FORMULATION DEVELOPMENT AND EVALUATION OF FAST DISSOLVING TABLETS OF TORSEMIDE

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ABSTRACT: Hypertension is a chronic disease that is characterized by a persistently high blood pressure. It can cause strokes, myocardial infarctions, heart failure, and chronic kidney failure if not treated properly. An effort has been made to develop a fast dissolving tablet containing torsemide, which is used in the treatment of hypertension, in enhancing the onset of action, therapeutic response, patient acceptance, and ease of access. Torsemide fast dissolving tablets (FDTs) were prepared by direct compression method using different ratios of super-disintegrants. The prepared tablets were subjected to both pre and post evaluation parameters including Fourier Transform Infrared spectroscopy (FT-IR), Differential Scanning Calorimetry, Micromeritics properties, Hardness, weight variation, friability, disintegration time, wetting time, water absorption ratio and in-vitro dissolution studies. FTIR studies showed that the drug and excipients are compatible. According to the micromeritics analysis, all formulations had acceptable to good flow ability. Tablet hardness and friability indicated that the prepared formulations were having good mechanical strength. The formulation F27 which was prepared by using of super-disintegrant Crospovidone gave the good results for tablet disintegration, wetting time, and water absorption ratio and in-vitro dissolution.

Keywords: Torsemide, Fast dissolving tablets, Super-disintegrants, Hypertension.

INTRODUCTION:

Oral mucosal drug delivery systems are frequently used as a novel site for drug administration, allowing for rapid and sustained release by avoiding first-pass metabolism and enzymatic destruction caused by gastrointestinal microbial flora. [1] Dysphagia or difficulty swallowing is ubiquitous in people of all ages. It affects approximately 35% of the general population, as well as another 30-40% of elderly hospitalized patients and 18-22% of all people in long-term care facilities. The size, surface, form, and flavor of tablets are the most common concerns concerning difficulties swallowing tablets, in order of frequency of complaints. Easy-to-swallow dosage forms are especially important for geriatric and pediatric patients.

Because of their convenience in terms of self-administration, compactness, and ease of manufacture, tablets have been the most often utilized dosage form even now. Elderly, juvenile, and mentally ill patients, on

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the other hand, have trouble swallowing conventional tablets, resulting in poor patient compliance. To tackle these issues, researcher developed a novel drug delivery mechanism called as rapid dissolving tablets (FDTs). The term orodispersible tablet was recently adopted by the European Pharmacopoeia to describe tablets that scatter quickly and within 3 minutes in the mouth before ingesting. When placed on the tongue, fast dissolving tablets instantly disintegrate, releasing the medication, which dissolves or disperses in the saliva. As saliva goes down into the stomach, some medications are absorbed from the mouth, throat, and oesophagus as well as travelers who may not have immediate access to water.

In such instances, drug bioavailability would be much higher than that seen with conventional tablet dosage regimens. Some medications' bioavailability may be improved as a result of drug absorption in the oral cavity as well as pregastric absorption of saliva containing dispersed pharmaceutical drugs that pass down into the stomach. [2] The drug's rapid solubility/ absorption, which may result in a quick beginning of action. [3] Hypertension is a major risk factor for cardiovascular illnesses, which are among the major causes of death in developed countries. The patient's adherence to the therapeutic regimen is necessary in the treatment of high blood pressure. The patient must adhere strictly to the schedule and not miss any doses.

The most prominent reasons for noncompliance or non-adherence to antihypertensive drugs are dysphagia and lack of water during travelling. In the treatment of hypertension, rapid start of action is a major concern. There is a significant decline in functional ability and acute restlessness in patients with suddenly raised blood pressure. To address these issues, a patient-friendly tablet, known as a fast-dissolving tablet (FDT), has been developed. Torsemide is a loop diuretic of the pyridine sulfonyl urea type used to treat hypertension and edema in congestive heart failure. It can be used alone or in conjunction with other diuretics such as thiazides.

MATERIALS REQUIRED:

Torsemide was procured as a gift sample from Micro labs (P) Ltd, Hosur. Sodium starch glycolate, Crospovidone and Croscarmellose sodium was obtained from Pharma Fabrikon, Madurai, India. Sodium lauryl sulphate was obtained from Rankem fertilizers & chemicals Ltd, New Delhi, India.

METHODOLOGY:

Drug-Excipients interaction studies:

The FT-IR spectrum of pure drug and formulated tablets were recorded on an Infrared spectrometer (Shimadzu, Japan) using KBr discs. The spectrum ranges 4000 to 400 cm^{-1}. [5]

ISSN: 2519-9889
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Differential scanning calorimetric (DSC) studies:

Differential scanning calorimetry was used for screening. Thermograms of Torsemide and final formulation were recorded by using Differential Scanning Calorimeter. The specified samples was hermetically sealed in a flat bottomed aluminium pans and heated in the differential scanning colorimeter (DSC Q200 V 24.4 Build 116) in an atmosphere of nitrogen and the rate of flow was 25ml/min, temperature range of 00 C to 2500 C was used and the heating rate was 100C/min.

PREPARATION OF TORSEMIDE FAST DISSOLVING TABLETS:

Different tablet formulations were prepared by direct compression technique. Drug, diluents, super disintegrants, surfactant and sweetener were passed through sieve#40. Magnesium stearate was passed through sieve#80. Required quantity of drug and surfactant was mixed first than other excipients were mixed thoroughly. Direct compression was used to compress the resulting powder using a cadmach compression machine with 6mm flat punches. [4] Tables 1A, 1B and 1C show the composition of all of the formulations.

Table 1A: Formulation of fast dissolving tablet of Torsemide

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Torsemide	5	5	5	5	5	5	5	5	5
Sodium starch glycolate	2	4	6	8	10	12	14	16	18
Croscarmellose sodium	-	-	-	-	-	-	-	-	-
Crospovidone	-	-	-	-	-	-	-	-	-
Mannitol	30	30	30	30	30	30	30	30	30
Microcrystalline cellulose	57.5	55.5	53.5	51.5	49.5	47.5	45.5	43.5	41.5
Sodium saccharin	2	2	2	2	2	2	2	2	2
Magnesium stearate	1	1	1	1	1	1	1	1	1
Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Peppermint flavour	1	1	1	1	1	1	1	1	1
Sodium lauryl sulphate	1	1	1	1	1	1	1	1	1

ISSN: 2519-9889
Impact Factor: 5.721

Table 1B: Formulation of fast dissolving tablet of Torsemide

Ingredients (mg)	F10	F11	F12	F13	F14	F15	F16	F17	F18
Torsemide	5	5	5	5	5	5	5	5	5
Sodium starch glycolate	-	-	-	-	-	-	-	-	-
Croscarmellose sodium	2	4	6	8	10	12	14	16	18
Crospovidone	-	-	-	-	-	-	-	-	-
Mannitol	30	30	30	30	30	30	30	30	30
Microcrystalline cellulose	57.5	55.5	53.5	51.5	49.5	47.5	45.5	43.5	41.5
Sodium saccharin	2	2	2	2	2	2	2	2	2
Magnesium stearate	1	1	1	1	1	1	1	1	1
Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Peppermint flavour	1	1	1	1	1	1	1	1	1
Sodium lauryl sulphate	1	1	1	1	1	1	1	1	1

Table 1C: Formulation of fast dissolving tablet of Torsemide

Ingredients (mg)	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28
Torsemide	5	5	5	5	5	5	5	5	5	5
Sodium starch glycolate	-	-	-	-	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	-	-	-	-	-	-	-
Crospovidone	2	4	6	8	10	12	14	16	18	-
Mannitol	30	30	30	30	30	30	30	30	30	30
Microcrystalline cellulose	49.5	47.5	45.5	43.5	41.5	57.5	55.5	53.5	51.5	53.5
Sodium saccharin	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	1	1	1	1	1	1	1	1	1	1
Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Peppermint flavour	1	1	1	1	1	1	1	1	1	1
Sodium lauryl sulphate	1	1	1	1	1	1	1	1	1	1

ISSN: 2519-9889
Impact Factor: 5.721

PRE-COMPRESSIONEVALUATION OF FAST DISSOLVING TABLETS

Angle of repose (θ)

Angle of repose was determined using fixed funnel method. The blend was poured via a funnel that could be elevated vertically until the maximum cone height (h) was reached. Radius of the heap(r) was measured and angle of repose was calculated using formula [6]

$$\theta = \tan^{-1}(h/r)$$

Where,

θ = angle of repose,

h = height of pile,

r = radius of the base pile.

Bulk density

Apparent bulk density (LBD) was determined by pouring blend into a graduated cylinder. The bulk volume (v_o) and weight of powder (m) was determined. The bulk density was calculated using the formula [7]

$$\mathbf{LBD} = \frac{\mathbf{weight\ of\ powder\ taken(m)}}{\mathbf{Bulk\ volume(vo)}}$$

Tapped density:

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (vt) occupied in the cylinder and weight of powder blend (m) was measured. The tapped density (TBD) was calculated using the formula [8]

$$\mathbf{TBD} = \frac{\mathbf{weight\ of\ powder\ taken(m)}}{\mathbf{Tapped\ volume(vt)}}$$

Carr's index (I)

The simplex way of measurement of the free flow of powder was compressibility, an indication of the ease with which a material can be induced to flow was given by compressibility index of the granules was determined by carr's compressibility index (c) which was calculated by using the following formula [9]

$$\mathbf{C} = \frac{\mathbf{TBD - LBD}}{\mathbf{TD}} \times \mathbf{100}$$

ISSN: 2519-9889
Impact Factor: 5.721

Hausner's ratio

Hausner ratio was an indirect index of ease of powder flow. It was calculated by the following formula.[9]

$$\textbf{Hausner's ratio} = \frac{\textbf{Tapped density(TBD)}}{\textbf{Bulk density(LBD)}}$$

Lower hausner ratios (<1.25) indicate better flow properties than higher ones (>1.25).

Drug content for powder blend:

The Powder blend containing 5 mg equivalent of drug weighed, dissolved and volume was made upto 100ml with 0.1N HCl solution. From the above solution, 5 ml was taken and diluted with 0.1N HCl to obtain (10µg/ml) concentration. The drug content was estimated by measuring the absorbance of the resulting solution at 288nm with a UV spectrophotometer (shimadzu UV-1700 pharma spec, Japan). [10]

POST COMPRESSION EVALUATION OF FAST DISSOLVING TABLETS

General appearance

Five tablets from different batches were randomly selected and organoleptic properties such as color, odor, taste, shape were evaluated. [11]

Thickness and Diameter

Thickness of tablet was determined using vernier caliper (Linker, Mumbai). Three tablets from each batch were used and an average value was calculated. [12]

Hardness

The tablet hardness, which was the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring and expressed in kg/cm^2 [13]

Weight variation

Weight variation test was done with 20 tablets. It was the individual variation of tablet weight from the average weight of 20 tablets. [12]

Wetting time

A simple procedure was used to determine the wetting time of the tablets. Five circular tissue papers, each with a diameter of 10cm, were positioned in a petridish with a diameter of 10cm. Ten millilitres of water that contains a water soluble pigment (eosin) was incorporated to the petridish. The tablet was carefully placed on the tissue paper's surface. The wetting time was defined as the time it took for water to reach the tablet's upper surface. [15]

ISSN: 2519-9889
Impact Factor: 5.721

Water absorption ratio

A piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighed. Water absorption ratio, R is determined using following equation

$$\mathbf{R = \frac{Wa - Wb}{Wb} \times 100}$$

Where,

Wa =Weight of tablet after water absorption

Wb= Weight of tablet before water absorption

In-vitro disintegration test

The disintegration test apparatus (Lab India Disso apparatus, 2000, India) was used to determine the in vitro disintegration time. A tablet was placed in the apparatus, and a disc was added to each of the six tubes. Suspend the basket rack in a beaker filled with 900 ml of distilled water at 37^0 C and move the basket, incorporating tablets, up and down 5-6 cm at a frequency of 28-32 cycles per minute. The time it took for the tablet to completely disintegrate, leaving no discernible mass in the apparatus, was measured in seconds. [16]

Disintegration time

a) Uncoated tablets: 5- 30 minutes

b) Coated tablets: 1-2 hours

c) Fast dissolving tablets: less than 3 minutes (European Pharmacopoeia)

In-vitro dissolution test

The drug release rate of Torsemide from fast dissolving tablets was determined using the USP dissolution test apparatus II (paddle type). The dissolution test was performed at 37 ± 0.5^0c and a rotation speed of 50 rpm, using 900ml of 0.1N Hcl as buffer solution. A sample of 5 ml of solution was withdrawn from the dissolution apparatus every 5 minutes for 30 minutes. Using a UV spectrophotometer, the absorbance of these solutions was measured at 288 nm. An equation derived from a standard curve was used to calculate cumulative percentage drug release. [17]

X-ray diffraction studies

Powder X-ray diffraction pattern of Torsemide, excipients and final formulation were studied using X-ray diffractometer (XRD-462, Digaku, Japan) with CuKα radiation. 40 kV and 30 mA were chosen as the voltage and current settings, respectively. With a scan speed of 10^o/min, all patterns were scanned over the range 5-70^o 2θ.

ISSN: 2519-9889
Impact Factor: 5.721

Stability studies

Three batches of the best formulation were stored for two months at at 40° C ± 2°C and RH 75% ± 5%. The drug content, physical appearance, hardness, and thickness of stored formulations were compared to those of freshly prepared tablets during in vitro release studies.

RESULTS AND DISCUSSION

Fourier Transform Infrared spectroscopic (FTIR) studies:

Infrared spectrum of pure drug showed the characteristic peaks at 3400.62 cm-1, 3348.54cm-1, 2968.55 cm-1, 1654.01 cm-1, 1462.09 cm-1, 1315.5 cm-1, 1083.07cm-1, 881.5 cm-1. Further in the fast dissolving tablet, all the above characteristics peaks of the drug appeared in the spectrum, which indicated that there was no interaction between the drug and excipients used in the formulation.

Differential scanning colorimetric (DSC) studies:

Any possible drug polymer interaction can be studied by thermal analysis. Torsemide's DSC thermogram was characteristic of a crystalline substance, with a sharp endothermic crest at 167.97^{o} C, which corresponded to melting and decomposition. The thermograms of the final formulation of torsemide with other excipients showed the existence of the drug endothermic peak which could indicate the absence of interactions between torsemide and other excipients. The thermogram of pure drug and fast dissolving tablet were shown in Figure 1 & Figure 2.

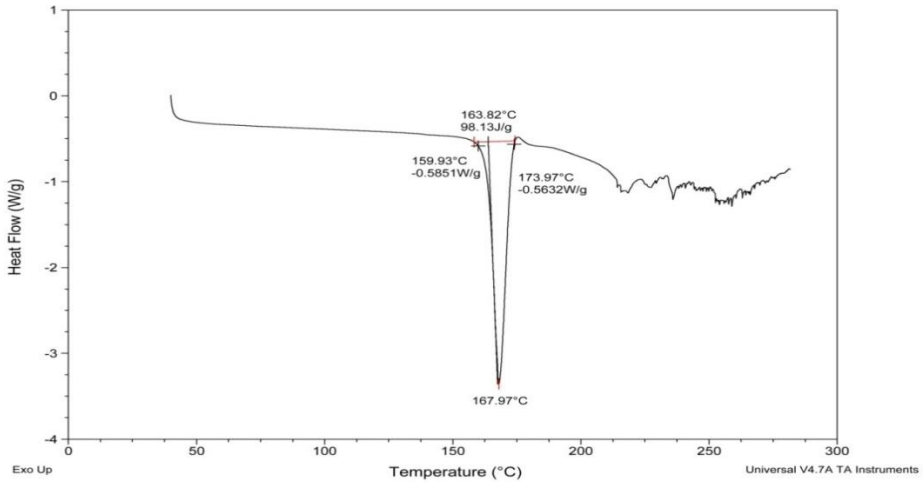

Figure 1: DSC thermogram of Torsemide

ISSN: 2519-9889
Impact Factor: 5.721

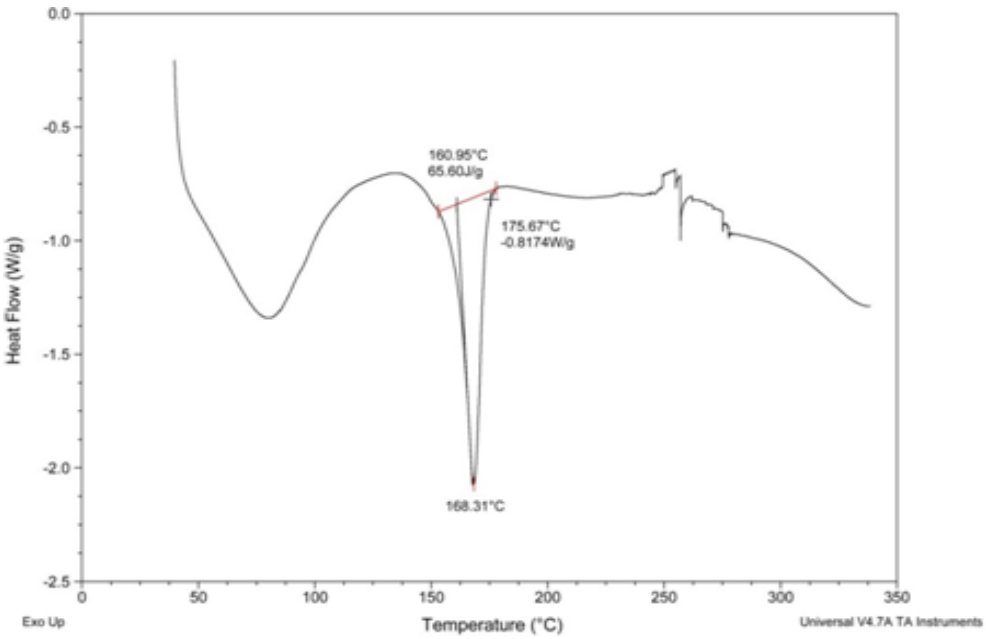

Figure 2: DSC thermogram of Torsemide fast dissolving tablet

Pre-compression evaluation for powder blend

To determine the flow properties of a powder blend, the pre-compression characteristics were evaluated for all formulations, i.e., F1 to F28. All of the formulations had an angle of repose ranging from 27°11' to 36°69' and a bulk density of 0.36–0.62 gm/ml. All formulations had tapped densities ranging from 0.43 to 0.69 g/ml, a compressibility index ranging from 7.13% to 25.01%, and a Hausner's ratio ranging from 1.07 to 1.33. The drug content in all of the formulations ranged from 97.04% to 101.49%.

Post compression evaluation of fast dissolving tablets

All the formulations exhibited a white color and a round shape, and the weight variation of FDTs was within acceptable limits. The Hardness of all formulations was found to be 3-4 kg/cm^2 and friability of all the formulation was ranged from 0.27 % to 0.83 %. All of the formulations had less than 1% friability, indicating that the tablets had good mechanical resistance. The thickness and diameter of all the formulations were used to determine the uniformity of size and shape of the tablets. From the results, it was found that the thickness of the tablet in all formulations was 3.0mm-3.2mm

ISSN: 2519-9889
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and the diameter of the tablet in all formulations was 6mm. The results show that all of the formulations were the same size and shape.

Wetting time

It was used to determine the capacity of the tablets to disintegrate by swelling of water. All the formulations showed quick wetting, this may be due to ability of swelling and also capacity of absorption of water. Table 3 shows the wetting time results for all formulations. The results showed that as the concentration of superdisintegrant increased, the time it took for the superdisintegrant to dissolve decreased. Formulation F27, which contains 18% Crospovidone, has a faster wetting time than the others, because of its action performed by the combination of both wicking and swelling mechanism.

In-vitro disintegration test

Formulations F1, F2, F3, F4, F5, F6, F7, F8, F9, F10, F11, F12, F13, F14, F15, F16, F17, F18, F19, F20, F21, F22, F23, F24, F25, F26, F27, F28 showed the disintegration time 146, 145, 136, 124, 114, 107, 98, 94, 87, 127, 119, 115, 110, 94, 87, 77, 82, 76, 94, 83, 74, 65, 71, 67, 64, 57, 53, 274 seconds respectively. It was observed that formulation F27, which contains 18% crospovidone, was found to disintegrate rapidly in a short period of time (53 seconds). The time it took for all of the tablets to disintegrate was less than 3 minutes (European Pharmacopoeia, 2001), indicating that they met the criteria for fast dissolving tablets. Table 3B summarizes the findings.

Table 2: Evaluation of mixed powder blend of Torsemide

Batch code	Angle of repose ± SD	Bulk density (g/ml)± SD	Tapped density (g/ml)±SD	Carr's index (%) ± SD	Hausner's ratio ± SD	Drug content (%)± SD
F1	31.58±4.27	0.42±0.00	0.52±0.00	20.01±0.05	1.24±0.00	95.70±1.20
F2	32.39±3.16	0.46±0.00	0.58±0.00	21.52±0.03	1.27±0.00	96.10±3.12
F3	29.92±1.62	0.45±0.00	0.57±0.00	20.02±0.03	1.25±0.00	95.00±1.47
F4	30.39±1.46	0.45±0.03	0.49±0.03	07.13±0.09	1.07±0.00	97.48±2.04
F5	33.53±1.62	0.62±0.03	0.69±0.04	09.67±0.48	1.10±0.00	95.98±3.01
F6	29.93±1.50	0.60±0.03	0.66±0.04	09.42±0.44	1.10±0.00	97.38±1.76
F7	30.91±0.32	0.45±0.05	0.51±0.05	12.78±0.48	1.14±0.00	97.68±1.42

ISSN: 2519-9889
Impact Factor: 5.721

F8	30.44±0.81	0.49±0.03	0.57±0.04	13.37±0.89	1.15±0.01	97.38±2.97
F9	30.17±0.28	0.48±0.01	0.55±0.02	13.05±0.48	1.14±0.00	98.69±0.17
F10	28.03±4.10	0.41±0.00	0.48±0.00	13.32±0.01	1.15±0.00	96.58±0.92
F11	27.11±3.37	0.41±0.00	0.48±0.00	13.32±0.00	1.15±0.00	97.68±1.42
F12	33.36±0.27	0.40±0.00	0.50±0.00	18.78±0.03	1.23±0.00	97.38±2.97
F13	30.39±0.35	0.42±0.00	0.52±0.00	19.99±0.06	1.24±0.00	98.69±0.17
F14	36.69±0.29	0.37±0.00	0.45±0.00	17.72±0.00	1.21±0.00	97.48±2.92
F15	30.73±0.50	0.36±0.00	0.43±0.00	16.70±0.00	1.20±0.00	95.77±4.13
F16	30.42±0.49	0.43±0.01	0.50±0.01	13.05±0.49	1.14±0.00	97.48±2.92
F17	30.23±0.67	0.44±0.03	0.51±0.04	13.37±0.90	1.15±0.01	98.19±0.30
F18	30.59±0.32	0.45±0.03	0.52±0.04	13.33±0.94	1.15±0.01	98.48±1.08
F19	30.60±0.44	0.41±0.00	0.55±0.00	25.01±0.06	1.33±0.00	97.58±1.20
F20	31.30±0.40	0.39±0.00	0.47±0.00	17.69±0.10	1.21±0.00	98.19±0.30
F21	30.33±0.57	0.39±0.01	0.47±0.02	18.00±0.64	1.21±0.01	98.08±1.13
F22	30.33±0.13	0.41±0.02	0.48±0.02	14.86±3.39	1.17±0.04	97.98±1.14
F23	30.33±0.32	0.41±0.01	0.48±0.02	14.58±3.60	1.17±0.05	97.98±1.48
F24	30.56±0.34	0.37±0.00	0.44±0.01	15.68±3.38	1.18±0.04	97.98±0.75
F25	30.95±0.27	0.45±0.03	0.49±0.03	07.13±0.09	1.07±0.00	98.59±1.05
F26	30.33±0.28	0.62±0.03	0.69±0.04	09.67±0.48	1.10±0.00	96.98±0.30
F27	30.98±0.46	0.60±0.03	0.66±0.04	09.42±0.44	1.10±0.00	99.19±0.62
F28	30.64±0.54	0.42±0.01	0.47±0.02	12.77±0.48	1.14±0.00	96.58±0.92

Table 3A: Evaluation of fast dissolving tablets of Torsemide

Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Average weight (mg)	Friability (%)	Content uniformity (%)
F1	3.2	3	99.20	0.83	98.39
F2	3.1	3	95.88	0.34	99.19

ISSN: 2519-9889
Impact Factor: 5.721

F3	3.1	3	98.16	0.58	98.79
F4	3.0	3	97.67	0.51	98.59
F5	3.2	3	98.36	0.41	98.39
F6	3.0	4	98.18	0.53	98.19
F7	3.1	3	98.70	0.41	97.88
F8	3.1	3	98.72	0.36	97.58
F9	3.1	3	98.48	0.35	98.09
F10	3.1	3	98.40	0.4	97.99
F11	3.2	3	98.79	0.43	97.98
F12	3.2	3	98.44	0.56	98.29
F13	3.1	4	98.44	0.32	98.08
F14	3.2	3	98.79	0.27	98.59
F15	3.2	4	97.50	0.52	98.19
F16	3.0	3	98.70	0.41	97.88
F17	3.0	3	98.5	0.31	98.59
F18	3.0	3	98.23	0.36	97.88
F19	3.0	3	93.68	0.3	98.59
F20	3.2	3	98.01	0.39	98.49
F21	3.2	4	97.69	0.37	98.09
F22	3.2	3	97.48	0.29	98.49
F23	3.1	3	98.08	0.28	97.88
F24	3.2	3	98.23	0.36	97.88
F25	3.0	3	97.48	0.29	98.49
F26	3.0	3	98.40	0.4	97.99
F27	3.0	3	98.79	0.43	97.98
F28	3.2	3	98.5	0.31	98.59

ISSN: 2519-9889
Impact Factor: 5.721

Table 3B: Evaluation of fast dissolving tablets of Torsemide

Formulation code	Disintegration time (sec)	Water absorption ratio (%)	Wetting time (sec)	Max % of drug release at 10 min
F1	146	50.45	118	93.09±0.54
F2	145	51.55	111	93.99±0.31
F3	136	58.19	102	92.17±0.54
F4	124	68.76	93	90.90±0.31
F5	114	75.03	79	90.53±0.54
F6	107	77.95	66	88.55±0.31
F7	98	79.31	52	96.34±0.31
F8	94	80.12	45	91.99±0.31
F9	87	83.1	34	95.09±0.31
F10	127	27.69	91	92.54±0.31
F11	119	41.39	82	90.56±0.54
F12	115	50.09	75	94.00±0.31
F13	110	50.58	68	84.75±0.31
F14	94	55.67	53	88.20±0.31
F15	87	58.86	47	92.73±0.54
F16	77	61.02	40	84.91±0.31
F17	82	60.38	31	91.27±0.31
F18	76	62.55	22	86.54±0.31
F19	94	62.36	51	92.55±0.31
F20	83	66.8	44	89.65±0.31
F21	74	76.07	39	92.74±0.54
F22	65	77.66	33	90.00±0.54
F23	71	79.52	29	89.10±0.31
F24	67	82.59	25	90.01±0.54
F25	64	85.91	19	95.98±0.54
F26	57	89.52	13	93.81±0.54
F27	53	91.9	10	99.62±0.31
F28	274	23.3	251	22.36±0.82

In-vitro dissolution test

The results showed that the release profiles of different formulations varied according to the type of superdisintegrants and its percentage in the formulations. Maximum percentage of drug (More than 80%) was

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released from the all formulations within 10 minutes. The maximum percentage of drug release was achieved by the formulation containing crospovidone (18%) as a superdisintegrant. It may be due to the results in the rapid disintegration of tablet in dissolution medium resulting in maximum drug release. The results were shown in Figure 3(a, b, c, d).

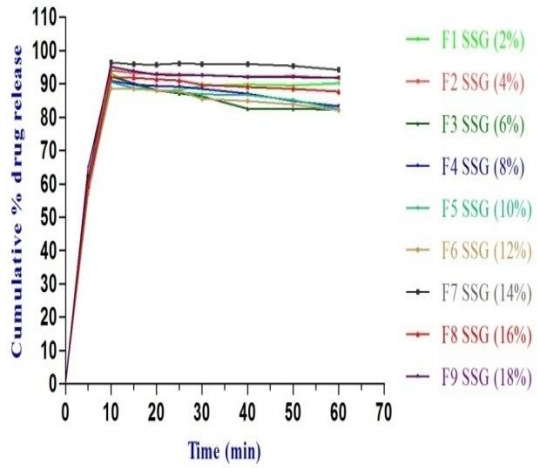

Figure 3 (a): In-vitro drug release profile of formulation batch F1-F9

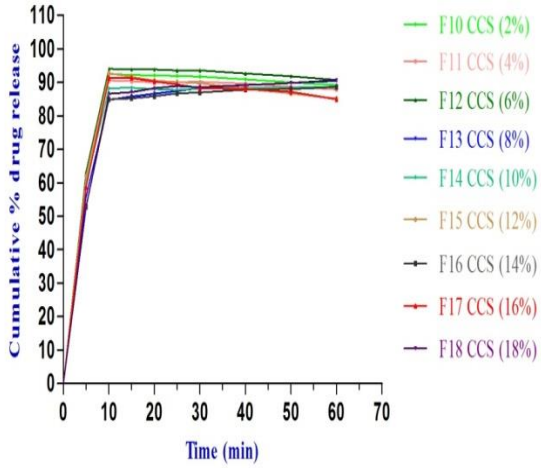

Figure 3 (b): In-vitro drug release profile of formulation batch F10-F18

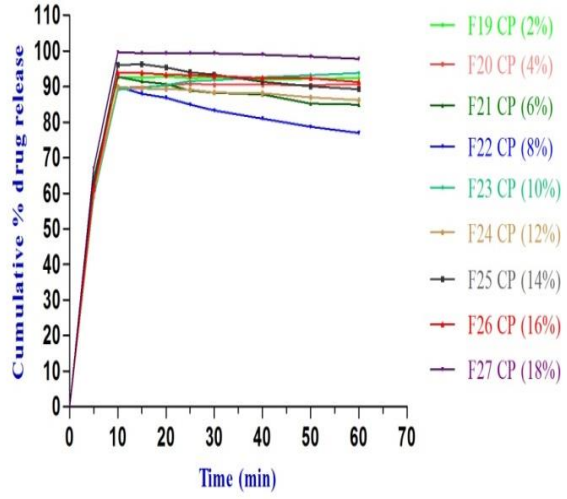

Figure 3 (c): In-vitro drug release profile of formulation batch F19-F27

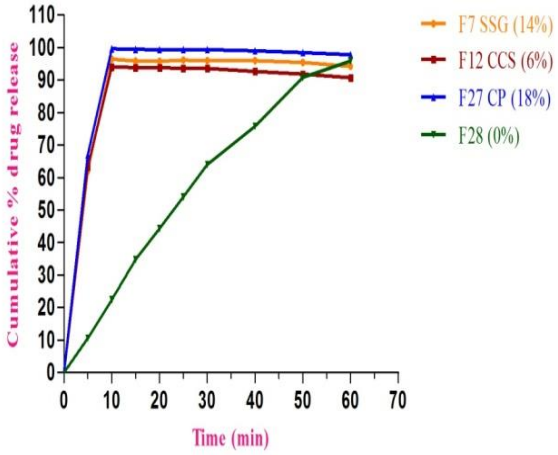

Figure 3 (d): Comparison of in-vitro release profile of different super disintegrants and without super disintegrants

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X-ray diffraction studies

Figure 4 depicts the PXRD graphs of torsemide, sodium starch glycolate, croscarmellose sodium, crospovidone, microcrystalline cellulose, sodium lauryl sulphate, and the best formulation (F27). The PXRD spectra of torsemide show numerous distinct crystalline peaks at 2 values of 6.13, 13.45, 17.63, 18.86, 20.88, 22.60, 23.55, 26.04, 28.11, and 28.65, indicating that torsemide is highly crystalline. The major X-ray diffraction peaks of the torsemide dispersible tablet formulation were reduced or absent, indicating that the crystallinity of the torsemide had reduced.

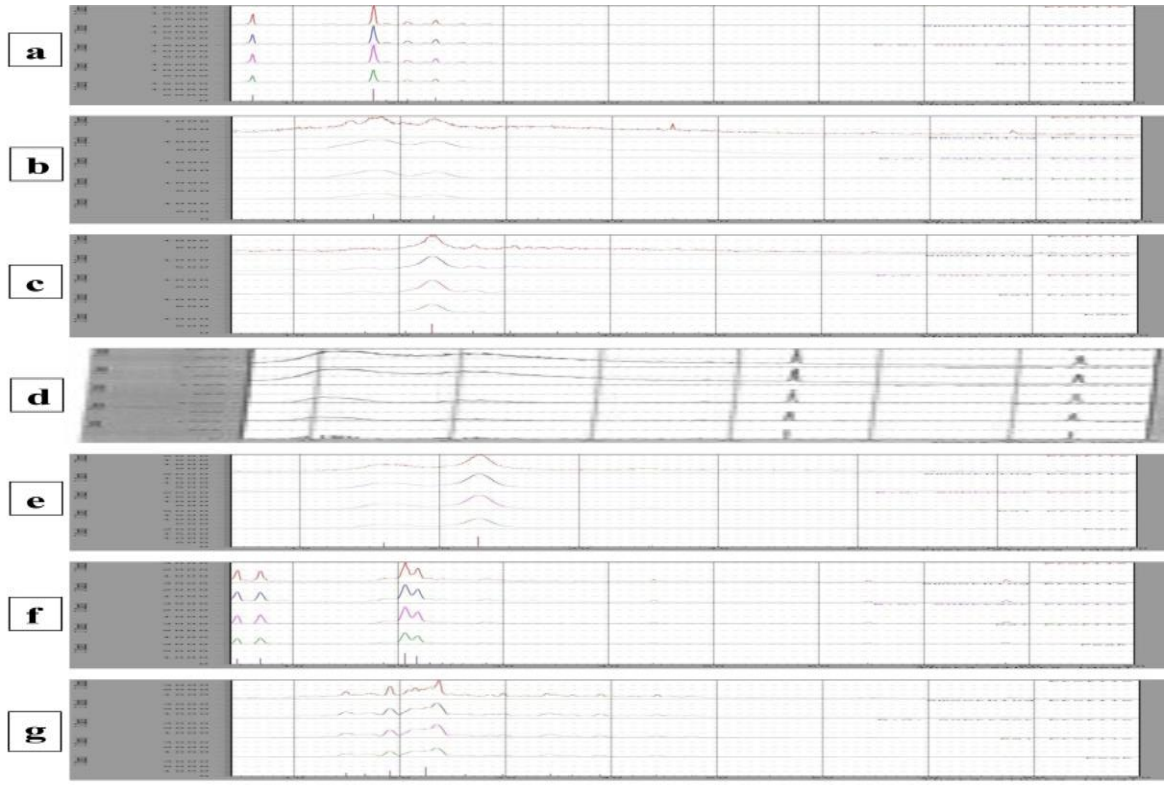

Figure 3: X-ray diffraction studies of (a) Torsemide (b) Sodium starch glycolate (c) Croscarmellose sodium (d) Crospovidone (e) Microcrystalline cellulose (f) Sodium lauryl sulphate (g) Torsemide fast dissolving tablet

Stability studies:

The best formulation of three batches is stored at 40° C ± 2°C and 75%± 5% RH for two months. The results showed no significant changes in physical appearance, hardness, thickness, drug content, wetting time, water absorption ratio, disintegration time and dissolution test of aged tablets compared to the fresh fast dissolving tablets. This indicates that the fast dissolving tablets were stable under these storage conditions. The results were shown in Table 4A & 4B.

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Table 4A: Stability study of best formulation (F27) at40° C ± 2°C and 75%± 5%

Parameters	Interval of testing		
	At 0 month	At 1month	At 2month
Physical appearance	White color	White color	White color
Hardness (kg/cm$^{2)}$	3	3	3
Thickness (mm)	3	3	3
Wetting time (sec)±SD*	10	14	15
Water absorption ratio(%)±SD*	91.90±0.57	91.39±0.59	91.20±0.43
Disintegration time (sec)±SD*	53	56	57
Drug content (%)±SD*	97.98±0.15	97.38±0.76	97.15±0.42

Table 4B: Dissolution profile of best formulation (F27) at 40° C ± 2°C and 75%± 5%

Time interval (min)	Percentage of drug release (%) ± SD*		
	At 0 month	At 1month	At 2month
5	66.92±0.54	65.65±0.31	65.29±0.54
10	99.62±0.31	98.53±0.31	98.17±0.54
15	99.45±0.31	98.35±0.31	98.17±0.54
20	99.27±0.00	98.17±0.54	97.99±0.32
25	99.28±0.00	98.17±0.54	97.80±0.32
30	99.27±0.00	98.16±0.54	97.79±0.32
40	98.91±0.31	97.61±1.08	97.42±0.83
50	98.36±0.30	97.59±1.09	97.22±0.63
60	97.80±0.31	97.03±0.55	96.83±0.32

n=3*

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CONCLUSION

It was concluded, that Torsemide can be successfully formulated as fast dissolving tablets with an objective to improve patient compliance and achieve rapid onset of action by direct compression method using various superdisintegrants, in different concentrations. The overall results revealed that the F27 formulation containing 18% crospovidone was excellent in terms of disintegration time and rate of dissolution. According to the stability study, there was no substantial shift in the selected formulation. Crospovidone can thus be used successfully in the composition of fast dissolving tablets.

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