INTRODUCTION

Mouth Dissolving Tablets [MDTs] dissolve or disintegrate in saliva and are swallowed without the need of water. MDTs offer an advantage over the conventional tablets because of their convenience of easy manufacturing, self-administration, Compactness. Therefore it improves the onset of action, increases bioavailability, and stability which helps to improve the choice of the dosage form in the current market [1, 2]. It also applies to people who are ill in bed, in traveling, and also those who are busy, especially those who have no access to water dissolves in the oral cavity within 15-3 min [3]. The demand for the development of Mouth Dissolving Tablets (MDTs) has hugely increased as it has better compliance in patients [4]. Mouth Dissolving Tablets are appreciated by a significant sector of the population, particularly those who have difficulty in swallowing. It has been reported that dysphasia [difficulty in swallowing] is common for all age groups and more specific with pediatric, geriatric populations along with institutionalized patients, psychiatric patients, and patients with nausea, vomiting, and motion sickness complications [5]. MDTs with good taste and flavor increase the acceptability of bitter drugs by various groups of the population [4, 5]. The ability to change the disease progress, cost-effectiveness, drug safety should be essential factors for all the treatments, and all these factors can be fulfilled by Mouth dissolving Tablets [6, 7]. Tofacitinib citrate is a Janus kinase JAK1/JAK3 inhibitor class [8]. It is currently developed by Pfizer for treating severe active rheumatoid arthritis in adult patients [9]. It is used for the treatment of severe active rheumatoid arthritis in adult patients, Ulcerative colitis, Psoriatic arthritis [10]. Janus kinases (JAKs) comprise a family of four enzymes, JAK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2), which are centrally working in cell signaling processes important in cancer and immune-inflammatory diseases. Progression in the Pharmaceutical field has taken a recent step forward with the approval of Tofacitinib [11]. Tofacitinib citrate is a citrate salt obtained by combining equimolar amounts of tofacitinib and citric acid. Tofacitinib act as a non-specific protein-tyrosine kinase inhibitor and an antirheumatic drug [12]. Also used to treat Atopic dermatitis, solid organ malignancy, and lymphoma in rheumatoid arthritis patients. The aim of this study to prepare mouth dissolving tablets of Tofacitinib Citrate used to treat certain types of arthritis [13].

MATERIALS AND METHODS

Material

Tofacitinib citrate gift sample was obtained from Formulation Development and Research Centre of Excellence, Unichem Laboratories Ltd., Goa-4035011, India. Sodium Starch Glycolate (SSG), Magnesium Stearate, Talc, Lactose was purchased from Mumbai, India [14]. The Tofacitinib citrate (Chemical Formula: C22H28N6O8) has 74% oral absorption produces absolute bioavailability, with peak plasma concentration (T max) achieved in 0.5-1 hour. The volume of distribution (Vd) = 87L after intravenous administration and has 40% protein binding, mostly bound to albumin. Distribution is equal between red blood cells and plasma half-life ~3h [15, 16].

Preparation of Ludiflash

Ludiflash is a simple mixture of 90 % w/w of Mannitol, 5 % w/w of Crospovidone, and 5 % w/w of polyvinyl acetate was blended in a double cone blender and was kept in an oven for 2 h drying. Active pharmaceutical ingredients lubricant and other ingredients were added in the above Ludiflash excipients which Produce high Porosity tablets and having quick penetration Power [17].

Method (Direct compression)

In this process, all ingredients were accurately weighed and passed through Sieve No.180 then mixed to form powder blend and then compressed using 6 mm flat punch on Tablet press 10 station
compression machine. The hardness of the tablets was maintained at 2-3 Kg/cm². Tablet weight was maintained at 75 mg [18, 19].

**Characterization of tofacitinib citrate**

**Determination of λmax**

For assurance of λmax stock solution Tofacitinib Citrate (conc. 1000 µg/ml) in 0.1 N HCl were prepared. 1 ml of the stock arrangement was additionally weakened to 100 ml. Coming about arrangements were examined in the range of 400 to 200 nm utilizing methanol as a clear with the assistance of a UV-visible spectrophotometer [20]. Normal triplicate readings were taken.

Calibration curve of tofacitinib citrate in pH 6.8 phosphate buffer

A stock solution of Tofacitinib Citrate was prepared by dissolving 100 mg of Tofacitinib Citrate in 100 ml of phosphate buffer pH 6.8, to obtain 1 mg/ml solution and from which 1 ml was withdrawn and diluted up to 100 ml with pH 6.8 Phosphate buffer to produce 10 ug/ml of solution. 10 ug/ml solution was scanned for wavelength at which maximum absorbance occurs λmax in a U. V. Spectrophotometer (Jasco V-630, Japan) between 200-400 nm. The λmax was found at 287 nm for Tofacitinib Citrate solution in phosphate buffer pH 6.8 and the same study was carried out in 0.1 N HCl, which shows maximum absorbance at 287 nm. Normal triplicate readings were taken [21].

**The partition coefficient of the drug**

Log P [22], was estimated utilizing a separating funnel by shaking equivalent volumes of oil and watery stage.

**Melting point identification**

The Melting purpose of Tofacitinib Citrate was resolved to utilize the open capillary technique [23].

**Formulation of a mouth dissolving tablet**

The mouth dissolving tablets of Tofacitinib Citrate was prepared by using 3² full factorial design [24, 25].

### Table 1: Formulae of tofacitinib citrate orally disintegrating tablets

| S. No. | Ingredients (mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|--------|------------------|----|----|----|----|----|----|----|----|----|
| 1.     | Tofacitinib Citrate | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| 2.     | Sodium Starch Glycolate | 5 | 5 | 5 | 10 | 10 | 15 | 15 | 15 | 15 |
| 3.     | Luidish | 20 | 30 | 40 | 20 | 30 | 40 | 20 | 30 | 40 |
| 4.     | Mag. Stearate | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 5.     | Talc | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| 6.     | Lactose | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |

### Pre-compression parameters of a powder blend

**Evaluation of pre-compression parameters**

**The angle of repose**

The frictional forces in a loose powder can be measured by the angle of repose. It is defined as the maximum angle possible between the surface of the pile of powder and the horizontal plane [26].

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

Where \( \theta \) is the angle of repose "h" is the height in cms, "r" is the radius in cms.

**Bulk density**

A Bulk density is determined by pouring pre sieved (180 mesh) bulk drug into a graduated cylinder via a large funnel and measuring the volume and weight. The average weight of triplicate readings was computed [26].

\[ \text{Bulk Density} = \frac{\text{Mass of powder (M)}}{\text{Bulk volume of the powder (V)}} \]

**Tapped density**

It is the ratio of the mass of granules to the volume of the granules after it is expressed by gm/cc [27].

\[ \text{Tapped Density} = \frac{\text{Weight of powder (W)}}{\text{Tapped volume of the powder (V)}} \]

**Carr's index**

Carr's Index was measured for the property of a powder to be compressed; as such, they are measured for the relative importance of inter particulate interactions. The average of Triplicate (three) readings was noted down [27].

\[ \text{Carr's index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100 \]

**Hausner's ratio**

This is the ratio of the poured density to the tapped density [28].

\[ \text{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}} \]

### Post-compression parameters

**Evaluation of post-compression parameters**

**Thickness and diameter**

The thickness of individual tablets was measured with a micrometer which permits accurate measurement and provides information on the variation between tablets [29].

**Hardness**

Tablet hardness is also called crushing strength of a tablet. It may be due to poor flow properties of the powder, moisture content of the powder. Monsanto hardness tester was used to check the hardness of the tablets [30].

**Friability**

Twenty tablets from each batch were selected randomly and weighed. These tablets were subjected to friability testing using a friabilator (Roch type) for 100 revolutions (25 rpm for 4 min.) Tablets were removed. De-dusted and weighed again. Average Triplicate readings were noted and SD was computed [31].

\[ \%F = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100 \]

**Weight variation**

The 29 tablets were selected at random and weighed on a Digital balance Average of three weights was calculated from the total weight. The percentage deviations from the mean value were calculated [32].

\[ \text{Weight Variation} = \left( \frac{w_1 - w_2}{w_2} \right) \times 100\% \]

Where \( w_1 \) is the initial weight of the tablet

\( w_2 \) is the average weight of the tablet

**Wetting time**

A petri dish containing 6 ml of 6.8 phosphate buffer was used. A tissue paper folded twice was kept in the dish and a tablet was placed on it. A small quantity of amaranth red color was put on the upper surface of the tablet. The time required for the upper surface
of the tablet to become red was noted as the wetting time of the tablet. An average of three readings was noted and standard deviation was computed [33].

**Determination of drug content**

Ten tablets from each formulation were powdered. The powder equivalent to 5 mg of Tofacitinib citrate was weighed and dissolved in acidic buffer pH 1.2 in 100 ml standard flasks. From this, suitable dilution was prepared and the solution was analyzed at 287 nm using a UV double beam Spectrophotometer using phosphate buffer PH 6.8 as blank [34].

**Disintegration test**

One Tablet was placed in each of the 6 tubes of the disintegration apparatus. An average of three readings was noted and standard deviation was computed [35].

**Dissolution test**

In vitro dissolution tests for all the formulations from F1-F9 were carried out by using modified dissolution apparatus [36, 37].

**RESULTS AND DISCUSSION**

**Result of pre-compression parameters**

The powder bed was evaluated for the rheological properties like bulk density. Tapped density, Angle of repose using standard pharmacopoeia techniques and from the results, Carr’s index, Hausner’s ratio were computed. Results of triplicate readings were averaged.

**Bulk density**

The apparent bulk densities for all formulated batches were found to be in between 0.54±0.023 gm/ml and 0.56±0.028 gm/ml Bulk densities were found in acceptable limits, which indicating that the packing properties required during compression are adequate in all formulations.

**Tapped density**

The values of tapped density were found to be in between 0.58±0.028 gm/ml and 0.62±0.011 gm/ml Tap densities were found in acceptable limit, which indicating that the packing properties required during compression are adequate in all formulations.

**Percentage carr’s index**

The values of percentage Carr’s index range from 6.06±2.602% to 82.46±0.323%, indicating that the blends have excellent compressibility.

**The angle of repose**

The angle of repose of all formulated batches was found to be between 21.44±0.965 and 23.63±4.602°, which implies good free-flowing nature of blends from hopper to die cavity.

**Table 2: Result of pre-compression parameters**

| S. No. | Parameter          | F1            | F2            | F3            | F4            | F5            | F6            | F7            | F8            | F9            |
|--------|--------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|
| 1.     | Bulk Density ±SD   | 0.58±0.01     | 0.54±0.192    | 0.55±0.01     | 0.54±0.04     | 0.56±0.089    | 0.54±0.04     | 0.57±0.01     | 0.58±0.186    | 0.54±0.097    |
| 2.     | Bulk Density ±SD   | 0.62±0.05     | 0.58±0.189    | 0.60±0.04     | 0.58±0.08     | 0.60±0.05     | 0.59±0.03    | 0.61±0.01     | 0.63±0.06     | 0.58±0.05     |
| 3.     | Bulk Density ±SD   | 6.41±0.04     | 7.5±0.026     | 8.246±0.05    | 7.36±0.04     | 7.17±0.06     | 9.27±0.01    | 6.06±0.05     | 7.34±0.18     | 7.36±0.03     |
| 4.     | Bulk Density ±SD   | 1.06±0.168    | 1.08±0.094    | 1.08±0.01     | 1.07±0.018    | 1.07±0.04    | 1.10±0.01    | 1.06±0.05     | 1.07±0.02     | 1.07±0.01     |
| 5.     | Bulk Density ±SD   | 23.6±0.02     | 21.6±0.04     | 22.44±0.01    | 21.63±0.06    | 21.66±0.07   | 22.58±0.195  | 22.63±0.08    | 23.15±0.01    | 23.16±0.06    |

**Result of post-compression parameters**

The mean thicknesses of all the formulations, F1 to F9 were found to be in the range of 2.02±0.13 to 2.31±0.45 mm and the tablet mean diameter of all formulations was found to be in the range of 6.01±0.01 to 6.09±0.06 mm. This indicated that the tablet production is consistent and reproducible. The hardness was found to be between the range of 2.24±0.01 to 2.67±0.005 kg/cm², indicating that tablets have good mechanical strength.

All the batches of all the formulation tablets were found to pass the weight variation test as the friability is less than 1% w/w. The formulations F1, F2, and F3 were prepared with 5 mg of SSG and 20 mg, 30 mg, and 40 mg Ludiflash, respectively. F1, F2, and F3 showed disintegration times of 59.6, 51and 44 sec respectively. The formulations F4, F5, and F6 were prepared with 10 mg of SSG and 20 mg, 30 mg, and 40 mg Ludiflash, respectively. F4, F5, and F6 showed disintegration times of 56.08, 50.74, and 43.68 sec respectively. The formulations F7, F8, and F9 were prepared with 15 mg of SSG and 20 mg, 30 mg, and 40 mg Ludiflash, respectively. F7, F8, and F9 showed disintegration times of 40.5, 37 and 29.75 sec respectively and wetting times 40.92, 29.61, and 27.89 sec respectively. The formulations F4, F5, and F6 were prepared with 10 mg of SSG and 20 mg, 30 mg, and 40 mg Ludiflash, respectively. F1, F2, and F3 showed disintegration times of 59.6, 51 and 44 sec respectively and wetting times of 40.92, 29.61, and 27.89 sec respectively. The results suggest that as the content of Ludiflash is increasing the disintegration time and wetting time of tablets decrease.

**Table 3: Result of post-compression parameters**

| S. No. | Batch code | Thickness (mm)±SD (n=3) | Diameter (mm)±SD (n=3) | Hardness (kg/cm²)±SD (n=3) | Weight variation±SD (n=3) | Friability %±SD (n=3) | Disintegration time (sec)±SD (n=3) |
|--------|------------|------------------------|------------------------|---------------------------|--------------------------|----------------------|-----------------------------------|
| 1.     | F1         | 2.1±0.001              | 6.053±0.066            | 2.24±0.01                 | 74.93±0.125              | 0.778±0.102          | 59.56±0.087                     |
| 2.     | F2         | 2.096±0.098            | 6.052±0.055            | 2.675±0.005               | 75.28±1.113              | 0.44±0.020           | 51.0±0.92                       |
| 3.     | F3         | 2.050±0.128            | 6.056±0.055            | 2.57±0.02                 | 75.76±0.577              | 0.41±0.095           | 44.0±1.48                       |
| 4.     | F4         | 2.313±0.452            | 6.01±0.011             | 2.463±0.005               | 75.8±0.507               | 0.770±0.169          | 48.0±0.92                       |
| 5.     | F5         | 2.09±0.084             | 6.056±0.060            | 2.523±0.005               | 73.4±1.732               | 0.636±0.048          | 45.7±0.01                       |
| 6.     | F6         | 2.04±0.113             | 6.053±0.064            | 2.39±0.01                 | 75.75±0.409              | 0.57±0.268           | 46.5±0.06                       |
| 7.     | F7         | 2.02±0.13              | 6.081±0.111            | 2.343±0.015               | 74.65±1.125              | 0.40±0.244           | 40.5±0.102                      |
| 8.     | F8         | 2.262±0.620            | 6.059±0.070            | 2.523±0.015               | 75.3167±1.284            | 0.772±0.154          | 37.0±0.68                       |
| 9.     | F9         | 2.15±0.049             | 6.097±0.066            | 2.33±0.01                 | 74.616±0.288             | 0.536±0.068          | 29.7±0.048                      |

Mean±SD, n=3
Result of *in vitro* drug release data of formulation F1-F3

### In vitro drug release data of formulation F1 (n=3)

The F1 formulation, containing 5 mg of SSG and 20 mg of Ludiflash, was found to release nearly 17% of the drug into dissolution fluid within the first 10 min. The drug release into dissolution media continues gradually and in 75 min it could release 84% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

### In vitro drug release data of formulation F3 (n=3)

The F3 formulation, containing 5 mg of SSG and 40 mg of Ludiflash was found to release nearly 22.90% of the drug into dissolution fluid within the first 10 min. The drug release into dissolution media continues gradually and in 60 min it could release 84.58% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

In the above discussion of F1, F2 and F3 containing 5 mg of SSG and varying amounts of Ludiflash 20 mg, 30 mg, and 40 mg, respectively, the release rate constant was found to increase in the following order F3>F2>F1 and the disintegration time was found to be F3<F2<F3.

### Table 4: Result of *in vitro* drug release data of formulation F1-F3

| S. No. | Time (min) | F1 Cumulative drug release (CDR)±SD (n=3) | Cumulative drug release % (%CDR)±SD (n=3) | F2 Cumulative drug release (CDR)±SD (n=3) | Cumulative drug release % (%CDR)±SD (n=3) | F3 Cumulative drug release (CDR)±SD (n=3) | Cumulative drug release % (%CDR)±SD (n=3) |
|--------|------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|------------------------------------------|
| 1      | 0          | 0.10±0.05                                | 0                                        | 0.10±0.05                                | 0                                        | 0.10±0.05                                | 0                                        |
| 2      | 1          | 0.25±0.05                                | 0.25±0.05                                | 0.25±0.05                                | 0.25±0.05                                | 0.25±0.05                                | 0.25±0.05                                |
| 3      | 5          | 0.45±0.05                                | 0.45±0.05                                | 0.45±0.05                                | 0.45±0.05                                | 0.45±0.05                                | 0.45±0.05                                |
| 5      | 10         | 0.69±0.05                                | 0.69±0.05                                | 0.69±0.05                                | 0.69±0.05                                | 0.69±0.05                                | 0.69±0.05                                |
| 15     | 30         | 1.00±0.05                                | 1.00±0.05                                | 1.00±0.05                                | 1.00±0.05                                | 1.00±0.05                                | 1.00±0.05                                |
| 45     | 60         | 1.20±0.05                                | 1.20±0.05                                | 1.20±0.05                                | 1.20±0.05                                | 1.20±0.05                                | 1.20±0.05                                |
| 75     | 60         | 1.80±0.05                                | 1.80±0.05                                | 1.80±0.05                                | 1.80±0.05                                | 1.80±0.05                                | 1.80±0.05                                |

*Data are expressed as mean ± SD (n=3)*

### Comparative *in vitro* drug release data of formulation F1-F3

The comparative study of dissolution profile of formulations F1, F2, and F3 was prepared with 5 mg of sodium starch glycolate and 20 mg, 30 mg, and 40 mg Ludiflash, respectively. Each of the tablets in all the formulations contains 5 mg of Tofacitinib citrate. The percentage release of drugs from F1, F2, and F3 were found to be 84.73%, 95.85%, and 101.90% in 75 min. Study respectively. The slope values of release data suggest that as the amount of Ludiflash increased rate of release of the drug gradually increases. The order of the above formulation was obtained in the following manner F3<F2>F1.

### Fig. 1: Comparative *in vitro* drug release profile of formulations F1-F3, *in vitro* drug release data of formulation F1-F3 (data represents mean±SD, n=3)

#### Result of *in vitro* drug release data of formulation F4-F6

### In vitro drug release data of formulation F4

The F4 formulation, containing 10 mg of SSG and 20 mg of Ludiflash was found to release nearly 21.26% of the drug into dissolution fluid within the first 10 min. The drug release into dissolution media continues gradually and in 75 min it could release 96.71% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

### In vitro drug release data of formulation F5

The F5 formulation, containing 10 mg of SSG and 30 mg of Ludiflash was found to release nearly 23.76% of the drug into dissolution fluid within the first 10 min. The drug release into dissolution media continues gradually and in 75 min it could release 96.71% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

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continues gradually and in 60 min it could release 83.51% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

**In vitro drug release data of formulation F6**

The F6 formulation, containing 10 mg of SSG and 40 mg of Ludiflash was found to release nearly 25.17% of the drug into dissolution fluid within the first 10 min. The drug release into dissolution media continues gradually and in 60 min it could release 91.87% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

In the above discussion of F4, F5 and F6 containing 10 mg of SSG and varying amounts of Ludiflash 20 mg, 30 mg, and 40 mg, respectively, the release rate constant was found to increase in the following order: F6 < F5 < F4, and the disintegration time was found to be F6 < F5 < F4.

### Table 5: In vitro drug release data of formulation F4-F6

| S. No. | Time (min) | F4 Cumulative drug release (%) ±SD (n=3) | F5 Cumulative drug release (%) ±SD (n=3) | F6 Cumulative drug release (%) ±SD (n=3) |
|--------|------------|----------------------------------------|----------------------------------------|----------------------------------------|
| 1      | 0          | 0 ±0                                   | 0 ±0                                   | 0 ±0                                   |
| 2      | 1          | 0.1064 ±0.094                          | 0.1407 ±0.056                          | 0.1476 ±0.093                          |
| 3      | 3          | 0.2630 ±0.079                          | 0.3377 ±0.056                          | 0.3387 ±0.122                          |
| 4      | 5          | 0.5372 ±0.095                          | 0.6117 ±0.163                          | 0.6049 ±0.18                          |
| 5      | 10         | 0.8454 ±0.087                          | 0.9459 ±0.195                          | 1.0065 ±0.064                          |
| 6      | 15         | 1.2296 ±0.034                          | 1.3739 ±0.026                          | 1.5244 ±0.069                          |
| 7      | 30         | 1.8238 ±0.017                          | 2.4906 ±0.048                          | 2.0291 ±0.083                          |
| 8      | 45         | 2.4749 ±0.025                          | 2.6459 ±0.182                          | 2.8846 ±0.067                          |
| 9      | 60         | 3.1580 ±0.085                          | 3.3219 ±0.059                          | 3.5678 ±0.054                          |
| 10     | 75         | 3.8446 ±0.074                          | 3.9986 ±0.087                          | 4.2516 ±0.029                          |

*Data are expressed as mean±SD (n=3)

**Comparative in vitro drug release data of formulation F4-F6**

The comparative study of dissolution profile of formulations F4, F5, and F6 was prepared with 10 mg of sodium starch glycolate and 20 mg, 30 mg, and 40 mg Ludiflash, respectively. Each of the tablets in all the formulations contains 5 mg of Tofacitinib Citrate. The basic in vitro data obtained were tabulated (table 9, 10, and 11); the percentage release of drugs from F4, F5, and F6 were found to be 96.71 %, 100 %, and 106 % in 75 min. Study respectively. The slope values of release data suggest that as the amount of Ludiflash increased rate of release of the drug gradually increases. The order of the above formulation was obtained in the following manner: F4 < F5 < F6.

**Result of in vitro drug release data of formulation F7-F9**

**In vitro drug release data of formulation F7 (n=3)**

The F7 formulation, containing 15 mg of SSG and 20 mg of Ludiflash was found to release nearly 26.70% of the drug into dissolution fluid within the first 10 min. The drug release into dissolution media continues gradually and in 60 min it could release 91.87% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

**In vitro drug release data of formulation F8**

The F8 formulation, containing 15 mg of SSG and 30 mg of Ludiflash was found to release nearly 39.03% of the drug into dissolution fluid within the first 10 min. The drug release into dissolution media continues gradually and in 60 min it could release 99.84% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

**In vitro drug release data of formulation F9**

The F9 formulation, containing 15 mg of SSG and 40 mg of Ludiflash was found to release nearly 39.57% of the drug into dissolution fluid within the first 10 min. The drug release into dissolution media continues gradually and in 30 min it could release 100% of the drug. The raw data obtained were subjected to regression analysis and cum % of drug release was plotted against time [38, 39].

In the above discussion of F7, F8 and F9, containing 15 mg of SSG and varying amounts of Ludiflash 20 mg, 30 mg, and 40 mg, respectively, the release rate constant was found to increase in the following order: F9 > F8 > F7, and the disintegration time was found to be F9 > F8 > F7.
Table 6: In vitro drug release data of formulation F7-F9

| S. No. | Time (min) | F7 Cumulative drug release (CDR)±SD (n=3) | F7 Cumulative drug release % (CDR)±SD (n=3) | F8 Cumulative drug release (CDR)±SD (n=3) | F8 Cumulative drug release % (CDR)±SD (n=3) | F9 Cumulative drug release (CDR)±SD (n=3) | F9 Cumulative drug release % (CDR)±SD (n=3) |
|--------|------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|-------------------------------------------|
| 1      | 0          | 0 ±0.00                                  | 0 ±0.00                                  | 0 ±0.00                                  | 0 ±0.00                                  | 0 ±0.00                                  | 0 ±0.00                                  |
| 2      | 0          | 0.1493±0.00                              | 3.7341±0.00                              | 0.1558±0.00                              | 3.9164±0.00                              | 0.1737±0.00                              | 4.3461±0.00                              |
| 3      | 0          | 0.3412±0.00                              | 8.5329±0.00                              | 0.6341±0.00                              | 15.95±0.00                               | 0.8344±0.00                              | 20.869±0.00                              |
| 4      | 0          | 0.6329±0.00                              | 15.83±0.00                               | 1.1495±0.00                              | 28.91±0.00                               | 1.5822±0.00                              | 39.57±0.00                               |
| 5      | 0          | 1.0677±0.00                              | 26.70±0.00                               | 1.684±0.00                               | 42.37±0.00                               | 2.35±0.00                                | 58.97±0.00                               |
| 6      | 0          | 1.6381±0.00                              | 40.97±0.00                               | 2.265±0.00                               | 56.95±0.00                               | 3.17±0.00                                | 79.39±0.00                               |
| 7      | 0          | 2.317±0.00                               | 57.96±0.00                               | 2.86±0.00                                | 72.91±0.00                               | 4.00±0.00                                | 100.20±0.00                              |
| 8      | 0          | 2.996±0.00                               | 74.99±0.00                               | 3.48±0.00                                | 87.58±0.00                               | -                                        | -                                        |
| 9      | 0          | 3.6735±0.00                              | 91.87±0.00                               | 3.95±0.00                                | 100.3±0.00                               | -                                        | -                                        |

Comparative in vitro drug release data of formulation F7-F9

The comparative study of dissolution profile of formulations F7, F8, and F9 was prepared with 15 mg of sodium starch glycolate and 20 mg, 30 mg, and 40 mg Ludiflash, respectively. Each of the tablets in all the formulations contain 5 mg of Tofacitinib Citrate. The percentage release of drugs from F7, F8, and F9 were found to be 91.87 %, 99.84 %, and 100 % in 60, 60, and 30 min. Study respectively. The slope values of release data suggest that as the amount of Ludiflash increased rate of release of the drug gradually increased. The order of the above formulation was obtained in the following manner F4<F5<F6.

Result of stability studies of F9 formulation: stability studies at 40 °C/75% RH

The stability of Tofacitinib citrate in the fast dissolving tablets was assessed according to ICH guidelines. Arrangements were made inside a stability chamber to induce stress of temperature and humidity simultaneously and uniformly and all the tablets were kept for study [40]. A temperature of 40 °C and relative humidity of 75%RH were selected, and the F9 formulation was selected as a model dosage form. Nearly 50 tablets of F9 were placed inside the stability chamber so that each tablet is separated and was exposed to 40 °C/75%RH. At the end of 24 h, 30 d, 60days, and 90 d, 3 tablets were removed randomly and were subjected to dissolution. The tablets were inspected surely for any chamber [41]. The dissolution profiles were obtained and the results of these formulations were compared with the dissolution profile of the tablet which was no exposure to stress [42]. The profiles of the formulation F9 were seen to remain similar, indicated by slope, visual inspection showed that there was no apparent effect of temperature/humidity a color, odor, etc. which given in table 7.

Table 7: Result of stability studies of F9 formulation

| S. No. | Time (min) | Day (d) 1st Cumulative drug release % (CDR)±SD (n=3) | Day (d) 30th Cumulative drug release % (CDR)±SD (n=3) | Day (d) 60th Cumulative drug release % (CDR)±SD (n=3) | Day (d) 90th Cumulative drug release % (CDR)±SD (n=3) |
|--------|------------|--------------------------------------------------|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| 1      | 0          | 0 ±0.00                                           | 0 ±0.00                                           | 0 ±0.00                                           | 0 ±0.00                                           |
| 2      | 1          | 4.346±0.00                                       | 4.119±0.00                                       | 4.351±0.00                                       | 4.348±0.00                                       |
| 3      | 1          | 20.849±0.00                                      | 20.521±0.00                                      | 20.743±0.00                                      | 20.899±0.00                                      |
| 4      | 1          | 39.531±0.00                                     | 39.111±0.00                                     | 39.222±0.00                                     | 40.022±0.00                                     |
| 5      | 1          | 58.962±0.00                                     | 58.544±0.00                                     | 58.814±0.00                                     | 59.271±0.00                                     |
| 6      | 1          | 79.376±0.00                                     | 78.671±0.00                                     | 79.194±0.00                                     | 79.680±0.00                                     |
| 7      | 1          | 100.169±0.00                                    | 99.506±0.00                                    | 99.995±0.00                                    | 100.359±0.00                                    |

Standard Deviation (SD) n=3, from the stability study data, it was clear that drug was stable in the optimized formulation for the study period.
Therefore it was concluded that the drug Tofacitinib Citrate formulation can retain its original potency for at least 2 years. The ICH guidelines require 6 months of study, but because of time constraint, the results of only 3 months study has been reported; the remaining studies would be reported elsewhere at a later time.

CONCLUSION

The concept of formulating Mouth Dissolving Tablets of Tofacitinib Citrate using super disintegrants offers a suitable and practical of faster disintegration and dissolution characteristics. Tofacitinib Citrate using super disintegrants offers a suitable and practical alternative for oral drug delivery system for immediate and sustained drug release.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

The authors declared that the No conflict of interest for the given Article.

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