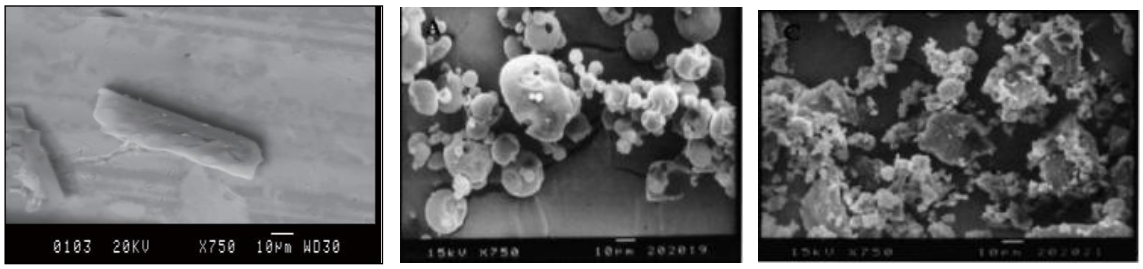


(A) (B) (C)

**Figure 7: SEM Photograph of Glimepiride-HP-β-CD inclusion complexes. (A) Glimepiride (B) HP-β-CD (C) Glimepiride-HP-β-CD kneaded complex (1:3M)**

**Table 5: Formulation of Glimepiride ODTs by direct compression method**

| INGREDIENTS | QUANTITY (mg) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ | $F_8$ | $F_9$ | $F_{10}$ |
| Glim+HP-β-CD (Equivalent to 4 mg of Glimepiride) | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 | 16 |
| Mannitol | 83 | 80 | 77 | 80 | 77 | 74 | 74 | 80 | 77 | 74 |
| M.C.C | 35 | 35 | 35 | 35 | 35 | 35 | 35 | 35 | 35 | 35 |
| Crospovidone | 9 | 9 | 9 | 12 | 12 | 12 | - | 12 | 12 | 12 |
| C.C.S | 6 | 9 | 12 | 6 | 9 | 12 | 12 | - | - | - |
| S.S.G | - | - | - | - | - | - | 12 | 6 | 9 | 12 |
| Aerosil | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Total** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** | **150** |

**Table 6: Evaluation of the powder blend of Glimepiride-HP-β-CD complexes containing excipients**

| Parameters | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ | $F_8$ | $F_9$ | $F_{10}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| Angle of repose(°) | 20’5” | 20’7” | 21’1” | 20’9” | 22’3” | 21’5” | 22’9” | 23’1” | 20’6” | 21’3” |
| Bulk density (g/cm$^3$) | 0.35 | 0.36 | 0.36 | 0.355 | 0.37 | 0.35 | 0.34 | 0.372 | 0.35 | 0.353 |
| Tapped density (g/cm$^3$) | 0.41 | 0.42 | 0.43 | 0.41 | 0.43 | 0.42 | 0.40 | 0.43 | 0.42 | 0.41 |
| Carrs Index (%) | 14.6 | 14.2 | 16.2 | 13.4 | 13.9 | 16.6 | 15 | 13.4 | 16.6 | 13.9 |
| Hausner’s ratio | 1.17 | 1.16 | 1.19 | 1.15 | 1.2 | 1.16 | 1.17 | 1.15 | 1.2 | 1.16 |
| Flowability | Good | Good | Good | Good | Good | Good | Good | Good | Good | Good |

**Table 7: Evaluation of directly compressible ODTs**

| Evaluation parameters | Batch code | | | | |
|---|---|---|---|---|---|
| | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ |
| Hardness (Kg/cm$^3$) | 3.1±0.16 | 2.8±0.17 | 3±0.13 | 3±0.15 | 3.1±0.19 |
| Thickness (mm) | 3.09±0.2 | 3.11±0.21 | 3.13±0.08 | 2.98±0.05 | 3.11±0.05 |
| Friability (%) | 0.38±0.11 | 0.39±0.09 | 0.38±0.12 | 0.42±0.08 | 0.41±0.06 |
| Weight variation | Passes | Passes | Passes | Passes | Passes |
| Wetting time (Sec) | 29 | 27 | 25 | 24 | 21 |
| Disintegration time (Sec) | 40 | 38 | 36 | 34 | 29 |
| Water absorption ratio | 22 | 21 | 20 | 20 | 19 |
| Drug content (%) | 99.90 | 101.32 | 99.98 | 102.36 | 103.56 |
| **Evaluation parameters** | **$F_6$** | **$F_7$** | **$F_8$** | **$F_9$** | **$F_{10}$** |
| Hardness (Kg/cm$^3$) | 3.5±0.20 | 2.8±0.25 | 3.5±0.21 | 3±0.15 | 3.1±0.09 |
| Thickness (mm) | 3.11±0.04 | 3.51±0.07 | 2.98±0.22 | 3.32±0.19 | 3.32±0.15 |
| Friability (%) | 0.41±0.05 | 0.38±0.05 | 0.42±0.05 | 0.40±0.08 | 0.40±0.07 |
| Weight variation | Passes | Passes | Passes | Passes | Passes |
| Wetting time (Sec) | 23 | 35 | 29 | 27 | 25 |
| Disintegration time (Sec) | 30 | 50 | 44 | 40 | 33 |
| Water absorption ratio | 20 | 23 | 21 | 20 | 20 |
| Drug content (%) | 101.43 | 99.89 | 99.78 | 101.2 | 99.98 |

inal morphology and shape of both Glimepiride andHP-β-CD are observed following complex formation and it is impossible to differentiate crystals of both

**Table 8: Dissolution parameters of directly compressible Orodispersible tablets**

| Time(min.) | % Drug release | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ | $F_8$ | $F_9$ | $F_{10}$ |
| **1** | 63.07 | 76.08 | 79.22 | 75.1 | 94.75 | 72.25 | 79.23 | 70.99 | 83.02 | 70.36 |
| **2** | 78.32 | 83.14 | 83.78 | 82.18 | 98.13 | 81.53 | 83.78 | 78.68 | 86.98 | 73.93 |
| **4** | 85.41 | 89.3 | 89.32 | 87.7 | 99.94 | 90.22 | 89.32 | 86.09 | 89.99 | 81.29 |
| **6** | 90.31 | 92.31 | 92.33 | 91.99 | 100.8 | 95.46 | 96.15 | 92.88 | 95.86 | 89.34 |
| **8** | 93.32 | 96.62 | 95.07 | 94.72 | 100.41 | 98.52 | 97.64 | 96.55 | 97.34 | 95.85 |
| **10** | 97.64 | 98.09 | 98.76 | 99.03 | 100.64 | 99.69 | 99.43 | 99.63 | 99.78 | 99.87 |

components which indicate an interaction of drug particles with HP-β-CD. This drastic change, indicative of the presence of a new solid phase, could be simply a consequence of a crystalline pattern change in this system and supports the existence of a new single phase.

**Dissolution Studies**

The Dissolution rate of GLIM alone and from cyclodextrin inclusion complexes were studied in pH 6.8 phosphate buffer (Fig.2,3) by maintaining sink condition are shown in (Table 3). It was found that complex prepared by Kneading method in 1:3 ratio showed best dissolution profile in comparison with respective Physical mixture and Co-grinding mixtures and pure drug GLIM. The Kneaded complex of Glimepiride showed 98.27% drug release in 15 minutes. The dissolution profiles were evaluated by dissolution efficiency parameter at 15 min ($DE_{15}$) and 30 min ($DE_{30}$) are shown in Table (3). The dissolution efficiency (DE) is defined by the area under the dissolution curve (AUC) at time, t. It is expressed as a percentage of the area of the rectangle corresponding to 100% dissolution, for the same total time, according to the following equation. (Khan KA, 1975):

$$DE = \frac{\int_0^t y \times dt}{y100 \times t} \times 100$$

Where, y is the percentage drug dissolved at time t.

The dissolution efficiency for kneaded complex (1:3M) ratio in 15 and 30 min. is 96% and 98% which was best in comparison to complexes prepared by Physical mixing and Co-grinding methods. It was also concluded that inclusion complex of drug prepared by Co-grinding method showed better dissolution profile in comparison to Physical mixture of drug.

The results for evaluation of different batches of Glimepiride ODTs by direct compression method are shown in Table 7. Properties like hardness, thickness, friability, weight variation and drug content of tablets of all the batches were found to be within acceptable limits.

Since mechanical integrity is of paramount importance in ODTs formulation, hence the hardness of the tablets was determined and was found to be in the range of 2.8 ± 0.25 to 3.5 ± 0.21 Kg/ $cm^3$. Friability was observed between 0.38 ± 0.11 to 0.42 ± 0.05, which were below 1% indicating sufficient mechanical integrity and strength of prepared tablets. The disintegration time for all formulations was found to be 21-35 seconds and wetting time was 19-23 seconds.

The rapid disintegration and wetting time was shown in the tablets containing combinations of Crospovidone and Croscarmellose sodium in concentrations of 8% and 6% respectively. Crospovidone exhibited high capillary action and pronounced hydration with little tendency to gel formation along with Croscarmellose sodium which attributes to rapid swelling and disintegration of tablets into apparently primary particles and proved to be the best combination.

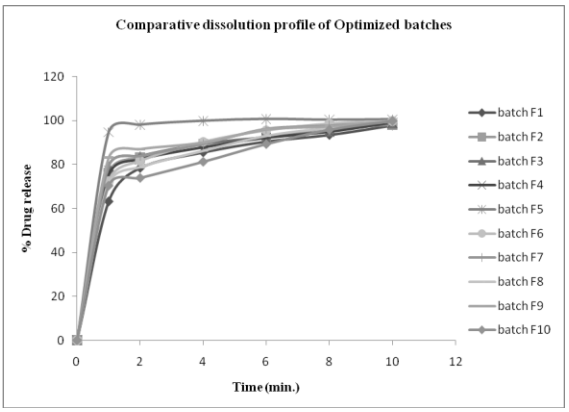


**Figure 8: Comparative dissolution profile of Optimized batches of Orodispersible tablets in 10 min**

Tablets of batch $F_5$ showed the least disintegration and wetting time followed by batches $F_6$, $F_{10}$, and $F_4$.The In-vitro dissolution studies were performed for all formulations and the results are shown in Table 7. In-vitro dissolution studies showed that more than 50% of the drug was released from all formulations within 5 minutes. The $F_5$ batch containing Crospovidone and Croscarmellose sodium in combination of 8% and 6% respectively had given the best dissolution profile than all other formulations i.e. 99.94% of drug release in 4 min as these superdisintegrants showed good compressibility, good compatibility, flowability and stability (Figure 8).

**CONCLUSION**

The data obtained from the present study demonstrated a significant improvement in solubility, dissolution rate and bioavailability of Glimepiride by its complexa-

tion with HPβCD. Inclusion complexes of GLIM and HP-β-CD (1:3M) prepared by kneading method exhibited higher rate of dissolution and higher dissolution efficiency value (DE) and appears to be the most valuable product for developing fast release orodispersible tablets of glimepiride along with the use of superdisintegrants, which can be useful in the treatment of Type 2 Diabetes Mellitus for quicker onset of action.

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