**Table 1: Weight compositions of different experimental bead formulations compressed into tablets**

| Formulation | Sugar beads: mesh size of 18-20 | Drug layer | | Hardening layer HPMC | Controlled release membrane layer (g) Surelease® solid content : Lactose | Outside most layer Lactose: Explotab = 2:1 | Compression pressure (lbs) | The total tablet weight (mg) |
|---|---|---|---|---|---|---|---|---|
| | | Glipizide | Surelease® solids content | | | | | |
| F1 | 67.5 g | 2.5 g | 5 g | 7.5 g | 7.5 g (100:5) | 0 g | 1500 | ~~396~~ |
| F2 | 67.5 g | 2.5 g | 5 g | 7.5 g | 7.5 g (100:5) | 10 g | 1500 | 440 |
| F3 | 67.5 g | 2.5 g | 5 g | 7.5 g | 7.5 g (100:5) | 15 g | 1500 | 462 |
| F4 | 67.5 g | 2.5 g | 5 g | 7.5 g (6.82%) | 7.5 g (100:5) | 20 g | 1000, 1500, 2000 | 484 |
| F5 | 70 g | 2.5 g | 5 g | 5 g (4.55%) | 7.5 g (100:5) | 20 g | 1500 | 484 |
| F6 | 71 g | 2.5 g | 5 g | 4 g (3.64%) | 7.5 g (100:5) | 20 g | 1500 | 484 |
| F7 | 70 g | 2.5 g | 5 g | 2.5 g (2.27%) | 7.5 g (100:5) | 20 g | 1500 | 484 |
| F8 | 70.625 g | 2.5 g | 4.375 g | 5 g | 7.5 g (100:5) | 20 g | 1000, 1500, 2000, 3000 | 484 |
| F9 | 70.625 g | 2.5 g | 4.375 g | 5 g | 6.0 g (100:7) | 20 g | 1500 | 484 |
| F10 | 70.625 g | 2.5 g | 4.375 g | 5 g | 5.4 g (100:7) | 20 g | 1500 | 484 |
| F11 | 70.625 g | 2.5 g | 4.375 g | 5 g | 5.4 g (100:10) | 20 g | 1500 | 484 |
| F12 | 71.25 g | 2.5 g | 3.75 g | 5 g | 5.4 g (100:7) | 20 g | 1500 | 484 |
| F13 | 71.25 g (64.77%) | 2.5 g (2.27%) | 3.75 g | 5 g | 7.5 g (100:7) | 20 g | 1500, 2000, 3000 | 484 |
| F14 | 76.25 g | 2.5 | 3.75 | 0 | 7.5 g (100:7) | 20 g | 1500 | 484 |

The numbers (e.g. 100:3) in parenthesis in the column of "Controlled release membrane layer" are the ratios of Surelease® solid content : lactose in each formulation. Batch size is 110 grams of coated~~ing~~ beads (the weights are the total in the batch). Percentage was calculated by taking weight of each coating layer divided by ~~based on~~ total ~~tablet~~ obtained beads weight. Obtained beads were compressed into tablets without adding any extra granular lubricants.

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**Table 2: Factors and levels studied for the influence of paddle speeds and compression pressures on release rate of F13 formulation**

| Factors | Code of factors | Levels |
|---|---|---|
| Compression pressures | Pressures | 1500, 2000 and 3000 pounds |
| Paddle speeds | rpm | 50, 100, 150 and 200 |

**Table 3: Effect of the amount of disintegrate applied on disintegration time of beads compressed into tablets observed during dissolution testing**

| Formulations | 11.11% of weight gain (F2) | 16.67% of weight gain (F3) | 22.22% of weight gain (F4) |
|---|---|---|---|
| Disintegration time | From 5h to more than 24 h | From 3 h to 20h. | From 2h to 3 h |

11.11%, 16.67% or 22.22% of weight gain of disintegrant layer in four layer coated beads.

**Table 4: ANOVA table for effect of the amount of binder/disintegrant applied on %release 16**

| | DF | Sum of square | Mean square | F value | Pr (F) |
|---|---|---|---|---|---|
| Model 1: %release16 ~ Weight gain of binder/disintegrant | | | | | |
| Weight gain | 1 | 1049.286 | 1049.286 | 21.021 | 0.003 |
| Residuals | 7 | 349.411 | 49.916 | | |

*DF = degree of freedom*

**Table 5: Multiple comparisons of effect of HPMC layer on percent (%) release at 16 hours by the Tukey's method (intervals excluding 0 are flagged by '****')**

| Comparison | Estimate | Standard Error | Lower bound | Upper Bound |
|---|---|---|---|---|
| F4 – F7 | 2.38 | 3.92 | -10.20 | 14.90 |
| F4 – F5 | -12.90 | 3.92 | -25.40 | -0.30**** |
| F4 – F6 | -6.00 | 3.92 | -18.60 | 6.55 |
| F7 – F5 | -15.20 | 3.92 | -27.80 | -2.67**** |
| F7 – F6 | -8.37 | 3.92 | -20.90 | 4.18 |
| F5 – F6 | 6.85 | 3.92 | -5.70 | 19.40 |

F4: 6.82% of HPMC; F5: 4.55% of HPMC; F6: 3.64% of HPMC; F7: 2.27% of HPMC

**Table 6: Multiple comparison of effect of Surelease layers on percent (%) release at 16 hours by the Tukey's method (intervals excluding 0 are flagged by '****')**

| Comparison | Estimate | Standard Error | Lower Bound | Upper Bound |
|---|---|---|---|---|
| F9 – F11 | -0.27 | 1.97 | -6.75 | 6.20 |
| F9 – F12 | -19.20 | 1.97 | -25.60 | -12.70**** |
| F9 – F13 | -9.59 | 1.97 | -16.10 | -3.12**** |
| F9 – F10 | -0.78 | 1.97 | -7.26 | 5.09 |
| F11 – F12 | -18.90 | 1.97 | -25.40 | -12.40**** |
| F11 – F13 | -9.32 | 1.97 | -15.80 | -2.84**** |
| F11 – F10 | -0.51 | 1.97 | -6.98 | 5.96 |
| F12 – F13 | 9.57 | 1.97 | 3.10 | 16.00**** |
| F12 – F10 | 18.40 | 1.97 | 11.90 | 24.80**** |
| F13 – F10 | 8.80 | 1.97 | 2.33 | 15.30**** |

F9: Surelease:drug = 1.75, and 6 g of Surelease:lactose = 100:7
F10: Surelease:drug = 1.75, and 5.4 g Surelease:lactose = 100:7
F11: Surelease:drug = 1.75, and 5.4 g Surelease:lactose = 100:10
F12: Surelease:drug = 1.5, and 5.4 g Surelease:lactose = 100:7
F13: Surelease:drug = 1.5, and 7.5 g Surelease:lactose = 100:7

**Table 7: Effects of compression pressures on friability and hardness tests of F8 (Requirement for friability test is less than 1%)**

| | Compression pressure (n = 10) | | | |
|---|---|---|---|---|
| | 1000 lbs | 1500 lbs | 2000 lbs | 3000 lbs |
| Friability test (% lost) | 1.22% | 0.72% | 0.36% | 0.29% |
| Hardness test (kg) | 4.17 ± 0.28 | 5.43 ± 0.57 | 6.0 ± 0.54 | 7.77 ± 0.27 |

**Table 8: ANOVA table for effect of compression pressures and paddle speeds on release rate from F13**

| | DF | Sum of square | Mean square | F value | Pr (F) |
|---|---|---|---|---|---|
| Model 2: release rate versus interaction between pressure and paddle speed | | | | | |
| Pressure | 2 | 0.135 | 0.068 | 1.026 | 0.374 |
| Speeds | 3 | 8.395 | 2.798 | 42.448 | < 0.001 |
| Pressure*Speeds | 6 | 1.601 | 0.267 | 4.047 | 0.006 |
| Residuals | 24 | 1.582 | 0.066 | | |

*DF = degree of freedom*

**Table 9: Two way ANOVA table for comparison of release rate between F13, 1500 pounds and Glucotrol® XL at different paddle speeds**

| | DF | Sum of square | Mean square | F value | Pr (F) |
|---|---|---|---|---|---|
| Model 3: Release rate ~ Gluco-F13 + Speed | | | | | |
| Gluco-F13 | 1 | 0.122 | 0.122 | 1.042 | 0.320 |
| Speed | 3 | 2.041 | 0.680 | 5.808 | 0.005 |
| Residuals | 19 | 2.225 | 0.117 | | |

*DF = degree of freedom; Gluco-F13 = Tablets have two levels (Glucotrol® XL versus F13, 1500 lbs).*

**Table 10: Comparison of dissolution profiles between Glucotrol® XL and F13, 1500 pounds; and F13 at different compression pressures**

| Comparison of Glucotrol® XL - F13, 1500 lbs | | Comparison of compression pressures for F13 at 100 rpm paddle speed | |
|---|---|---|---|
| Paddle speeds | f2 | Compression pressure | f2 |
| 50 rpm | 52.4 | 1500 lbs -2000 lbs | 52.1 |
| 100 rpm | 68.2 | 1500 lbs -3000 lbs | 57.4 |
| 150 rpm | 54.6 | 2000 lbs -3000 lbs | 69.9 |
| 200 rpm | 50.2 | | |