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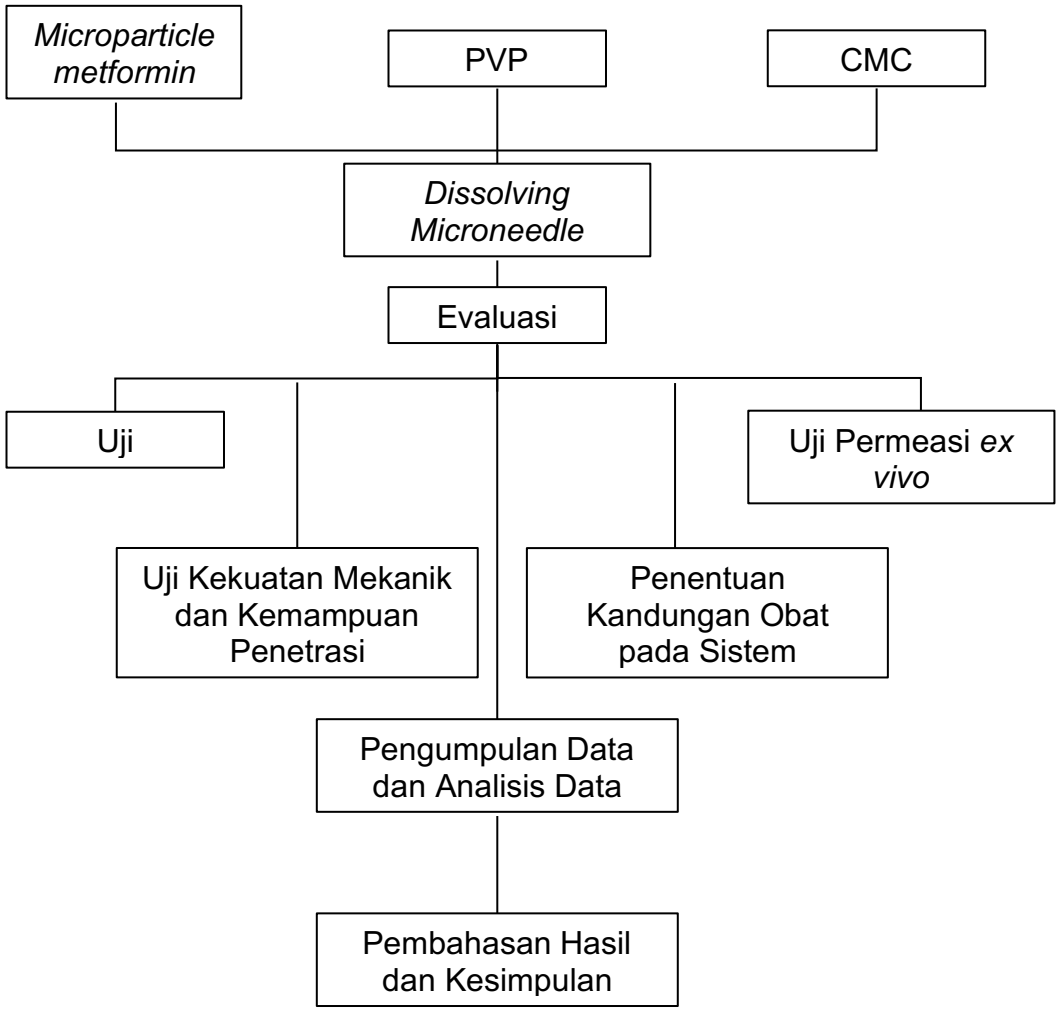
# LAMPIRAN

**Lampiran 1. Skema Kerja**



## Lampiran 2. Hasil Uji Morfologi, Kekuatan Mekanik dan Kemampuan Penetrasi *Dissolving Microneedle*

**Tabel 7. Persentase penurunan panjang *microneedle***

| Formula | Sebelum Uji Kekuatan Mekanik | | | Setelah Uji Kekuatan Mekanik | | | %penurunan panjang *needle* | Rata-rata | SD |
|---|---|---|---|---|---|---|---|---|---|
| | Panjang (µm) | Rata-rata | SD | Panjang (µm) | Rata-rata | SD | | | |
| DMNM1 | 701 | 700 | 1 | 531 | 528,3 | 11,24 | 24,25 | 24,52 | 1,64 |
| | 699 | | | 538 | | | 23,03 | | |
| | 700 | | | 516 | | | 26,28 | | |
| DMNM2 | 705 | 702 | 3 | 643 | 634,3 | 13,32 | 8,79 | 9,64 | 1,56 |
| | 702 | | | 641 | | | 8,68 | | |
| | 699 | | | 619 | | | 11,44 | | |
| DMNM3 | 698 | 698,3 | 1,53 | 678 | 656 | 19,97 | 2,86 | 6,06 | 2,96 |
| | 697 | | | 651 | | | 6,59 | | |
| | 700 | | | 639 | | | 8,71 | | |

**Tabel 8. Persentase penetrasi *dissolving microneedle***

| Lapisan | Jumlah lubang yang terbentuk | | | %penetrasi | | |
|---|---|---|---|---|---|---|
| | DMNM1 | DMNM2 | DMNM3 | DMNM1 | DMNM2 | DMNM3 |
| 1 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | 63,67 | 96 | 96 | 63,67 | 96 | 96 |
| 3 | 33 | 88,67 | 62 | 33 | 88,67 | 62 |
| 4 | 0 | 76,3 | 16,67 | 0 | 76,3 | 16,67 |
| 5 | 0 | 0 | 0 | 0 | 0 | 0 |
| 6 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7 | 0 | 0 | 0 | 0 | 0 | 0 |
| 8 | 0 | 0 | 0 | 0 | 0 | 0 |

### a. Contoh perhitungan persentase penurunn tinggi *microneedle*

Diketahui :

Tinggi *needle* DMNM2 sebelum uji: 705

Tinggi *needle* DMNM2 sesudah uji: 643

Persamaan yang digunakan:

$$\%\text{kompresi} = \frac{tinggi\ sebelum\ uji - tingi\ sesudah\ uji}{tinggi\ sebelum\ uji} \times 100\%$$

Sehinga

$$\%\text{kompresi} = \frac{705 - 643}{705} \times 100\%$$

$$= 8{,}79\%$$

**b. Perhitungan persentase penetrasi lapisan ke-n**

Diketahui :

Jumlah lubang DMNM2 pada lapisan ke-4 : 77

Jumlah lubang total : 100

Persamaan yang digunakan

$$\%\text{penetrasi} = \frac{Jumlah\ lubang\ pada\ lapisan\ ke{-}n}{Jumlah\ lubang\ total} \times 100\%$$

Sehingga

$$\%\text{penetrasi} = \frac{77}{100} \times 100\%$$

$$= 77\%$$

## Lampiran 3. Hasil Penentuan Densitas

**Tabel 9. Bobot setiap bahan dalam formula DMNM1, DMNM2 dan DMNM3**

| Bahan | DMNM1 | DMNM2 | DMNM3 |
|---|---|---|---|
| PVP | 25 | 25 | 25 |
| CMC | 1 | 2 | 3 |
| Mikropartikel Metformin | 25 | 25 | 25 |
| Air | 49 | 48 | 47 |

**Tabel 10. Bobot basah dan bobot kering sampel balok pipih campuran bahan DMNM1, DMNM2 dan DMNM3**

| Replikasi | Bobot basah (mg) | | | Bobot kering (mg) | | |
|---|---|---|---|---|---|---|
| | DMNM1 | DMNM2 | DMNM3 | DMNM1 | DMNM2 | DMNM3 |
| 1 | 495 | 513 | 503 | 275 | 291 | 290 |
| 2 | 514 | 516 | 509 | 286 | 292 | 294 |
| 3 | 506 | 518 | 518 | 281 | 293 | 299 |

**Tabel 11. Densitas**

| Formula | Panjang (mm) | Lebar (mm) | Tinggi (mm) | Volume ($mm^3$) | Bobot (mg) | Densitas (mg/ $mm^3$) | Rata-rata | SD |
|---|---|---|---|---|---|---|---|---|
| DMNM1 | 10 | 10 | 5,74 | 537,77 | 616,32 | 1,07 | 1,08 | 0,11 |
| | 10 | 10 | 6,25 | 624,81 | 618,00 | 0,99 | | |
| | 10 | 10 | 6,15 | 614,88 | 738,05 | 1,20 | | |
| DMNM2 | 10 | 10 | 5,56 | 555,78 | 595,11 | 1,07 | 1,09 | 0,11 |
| | 10 | 10 | 5,98 | 598,29 | 595,11 | 0,99 | | |
| | 10 | 10 | 5,91 | 590,95 | 719,54 | 1,22 | | |
| DMNM3 | 10 | 10 | 5,21 | 520.79 | 554,80 | 1,06 | 1,10 | 0,10 |
| | 10 | 10 | 5,51 | 550,56 | 562,86 | 1,02 | | |
| | 10 | 10 | 5,43 | 543,09 | 659,06 | 1,21 | | |

**a. Contoh perhitungan volume**

Diketahui

Panjang DMNM2 = 10

Lebar DMNM2 = 10

Tinggi DMNM2 = 5,56

Persamaan yang digunakan:

Volume = panjang x lebar x tinggi

Sehingga

= 10 mm x 10 mm x 5,56 mm

= 556 $mm^3$

**b. Contoh perhitungan densitas**

Diketahui :

Volume DMNM2 : 556 $mm^3$

Bobot DMNM2 : 595,11 mg

Rumus yang digunakan :

$$= \frac{bobot}{volume}$$

Sehingga

$$= \frac{595{,}11\ mg}{556\ mm3}$$

= 1,07

## Lampiran 4. Hasil Penentuan LOD dan Persentase Jumlah Mikropartikel Metformin dalam Massa Kering

**Tabel 12. Persentase kehilangan air**

| Replikasi | DMNM1 | DMNM2 | DMNM3 |
|---|---|---|---|
| 1 | 44,38 | 43,35 | 42,32 |
| 2 | 44,38 | 43,35 | 42,32 |
| 3 | 44,38 | 43,35 | 42,32 |

**Tabel 13. Persentase mikropartikel metformin dalam massa kering**

| Replikasi | DMNM1 | DMNM2 | DMNM3 |
|---|---|---|---|
| 1 | 44,95 | 44,13 | 43,34 |
| 2 | 44,95 | 44,13 | 43,34 |
| 3 | 44,95 | 44,13 | 43,34 |

### a. Contoh perhitungan LOD

Diketahui:

Bobot basah DMNM2 = 513

Bobot kering DMNM2 =291

Persamaan yang digunakan

$$\%LOD = \frac{bobot\ basah - bobot\ kering}{bobot\ basah} \times 100\%$$

Sehingga

$$= \frac{513-290}{513} \times 100\%$$

$= \frac{513-290}{513}$ x 100%

= 43,35%

**b. Contoh perhitungan persentase jumlah *glucose-response microparticle* metformin dalam massa kering**

Diketahui:

Bobot mikropartikel metformin awal dalam formula = 25%

LOD = 43,35%

Persamaan yang digunakan:

%jumlah *glucose response microparticle* metformin dalam masa kering= $\frac{bobot\ metformin}{100-43,35\%}$ x 100%

Sehingga

%jumlah *glucose response microparticle* metformin dalam masa kering= $\frac{25}{100-43,35\%}$ x 100%

= 44,13%

## Lampiran 5. Hasil Penentuan Volume, Bobot Jarum (*Needle*), dan Bobot Mikropartikel Metformin

**Tabel 14. Bobot 100 *needle* dalam massa kering**

| Replikasi | DMNM1 | DMNM2 | DMNM3 |
|---|---|---|---|
| 1 | 1,00 | 0,99 | 0,99 |
| 2 | 0,92 | 0,93 | 0,95 |
| 3 | 1,12 | 1,14 | 1,13 |

**Tabel 15. Jumlah *glucose-response microparticle* metformin dalam 100 *needle***

| Formula | Jumlah mikropartikel (mg) | Rata-rata | SD |
|---|---|---|---|
| DMNM1 | 0,45 | 0,46 | 0,044 |
| | 0,41 | | |
| | 0,50 | | |
| DMNM2 | 0,44 | 0,45 | 0,046 |
| | 0,41 | | |
| | 0,50 | | |
| DMNM3 | 0,43 | 0,44 | 0,040 |
| | 0,41 | | |
| | 0,49 | | |

**Contoh perhitungan penentuan volume, bobot jarum (*needle*), dan bobot metformin**

Diketahui:

Volume satu *needle* = 0,00934mm$^3$

Volume 100 *needle* = 0,00934 mm$^3$ x 100 = 0,943 mm$^3$

Bobot 100 *needle* = volume 100 *needle* x densitas

= 0,943 mm$^3$ x 1,07

= 1,009 mg

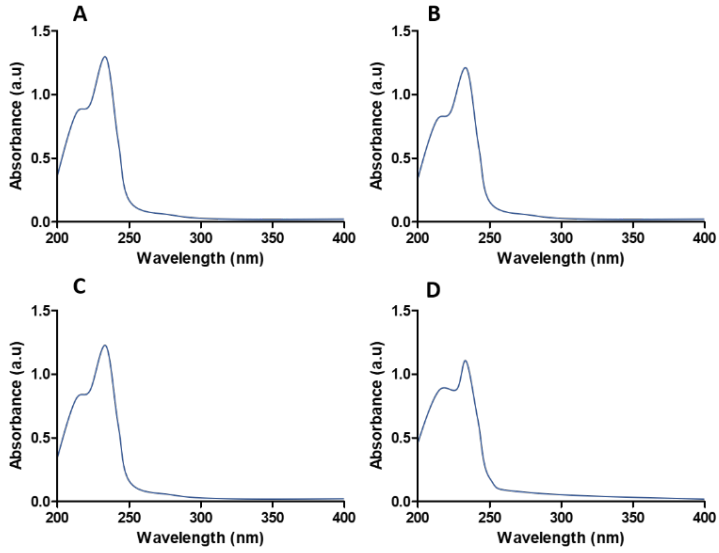
Jumlah *glucose-response microparticle* metformin dalam massa kering formula DMNM1

= %*glucose response microparticle* metformin x bobot 100 *needle*

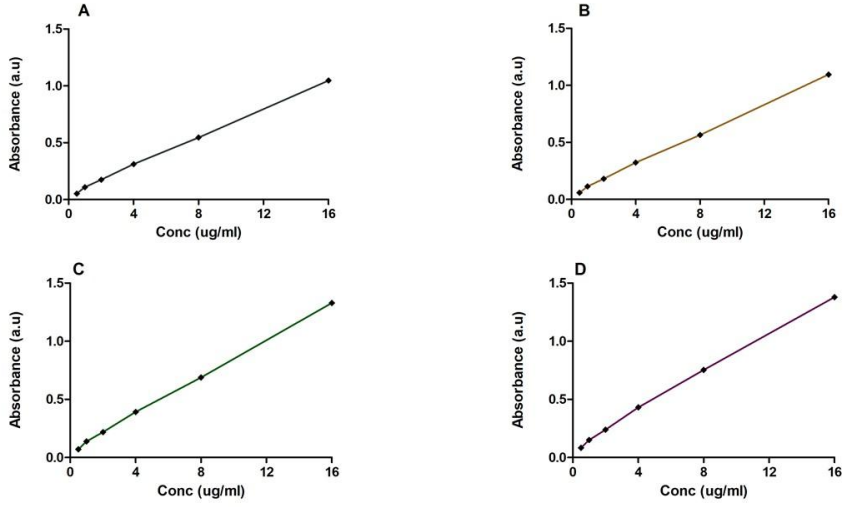
= 44,13% x 1,009

= 0,44 mg

## Lampiran 6. Hasil Penentuan Kandungan Obat pada Sistem *Microneedle*




Gambar 14. Panjang gelombang maksimum metformin di media PBS (A), PBS+glukosa 1% (B), PBS + glukosa 2% (C), dan PBS + glukosa 4% (D).




Gambar 15. Kurva baku metformin di media PBS (A), PBS+glukosa 1% (B), PBS + glukosa 2% (C), dan PBS + glukosa 4% (D).

**Tabel 16. Pembuatan kurva baku di media PBS**

| Konsentrasi | Absorbansi 1 | Absorbansi 2 | Absorbansi 3 | Rata-rata | SD |
|---|---|---|---|---|---|
| 0,5 | 0,053 | 0,055 | 0,051 | 0,053 | 0,001 |
| 1 | 0,111 | 0,105 | 0,133 | 0,109 | 0,003 |
| 2 | 0,178 | 0,174 | 0,169 | 0,174 | 0,004 |
| 4 | 0,313 | 0,315 | 0,306 | 0,312 | 0,005 |
| 8 | 0,546 | 0,538 | 0,551 | 0,545 | 0,006 |
| 16 | 1,053 | 1,037 | 1,050 | 1,047 | 0,008 |

**Tabel 17. Pembuatan kurva baku di media PBS + glukosa 1%**

| Konsentrasi | Absorbansi 1 | Absorbansi 2 | Absorbansi 3 | Rata-rata | SD |
|---|---|---|---|---|---|
| 0,5 | 0,066 | 0,056 | 0,053 | 0,058 | 0,006 |
| 1 | 0,116 | 0,107 | 0,117 | 0,113 | 0,005 |
| 2 | 0,187 | 0,177 | 0,176 | 0,180 | 0,005 |
| 4 | 0,329 | 0,322 | 0,318 | 0,323 | 0,005 |
| 8 | 0,573 | 0,549 | 0,574 | 0,565 | 0,014 |
| 16 | 1,105 | 1,088 | 1,092 | 1,095 | 0,009 |

**Tabel 18. Pembuatan kurva baku di media PBS + glukosa 2%**

| Konsentrasi | Absorbansi 1 | Absorbansi 2 | Absorbansi 3 | Rata-rata | SD |
|---|---|---|---|---|---|
| 0,5 | 0,071 | 0,060 | 0,079 | 0,070 | 0,009 |
| 1 | 0,125 | 0,115 | 0,174 | 0,138 | 0,032 |
| 2 | 0,201 | 0,190 | 0,262 | 0,218 | 0,038 |
| 4 | 0,355 | 0,345 | 0,474 | 0,392 | 0,071 |
| 8 | 0,619 | 0,589 | 0,855 | 0,688 | 0,145 |
| 16 | 1,194 | 1,167 | 1,627 | 1,329 | 0,258 |

**Tabel 19. Pembuatan kurva baku di media PBS + glukosa 4%**

| Konsentrasi | Absorbansi 1 | Absorbansi 2 | Absorbansi 3 | Rata-rata | SD |
|---|---|---|---|---|---|
| 0,5 | 0,091 | 0,080 | 0,078 | 0,083 | 0,007 |
| 1 | 0,129 | 0,153 | 0,171 | 0,151 | 0,021 |
| 2 | 0,207 | 0,253 | 0,257 | 0,239 | 0,028 |
| 4 | 0,366 | 0,459 | 0,465 | 0,430 | 0,055 |
| 8 | 0,638 | 0,784 | 0,837 | 0,753 | 0,103 |
| 16 | 1,331 | 1,398 | 1,412 | 1,380 | 0,043 |

**Tabel 20. Kandungan *glucose response microparticle* metformin dalam *needle***

| Formula | Mikropartikel dalam massa kering | Bobot *needle* kering | Jumlah *microparticle* metformin (mg) | Rata-rata | SD |
|---|---|---|---|---|---|
| DMNM 1 | 44,95 | 1,00 | 0,045 | 0,45 | 0,04 |
| | 44,95 | 0,92 | 0,41 | | |
| | 44,95 | 1,12 | 0,50 | | |
| DMNM 2 | 44,13 | 0,99 | 0,44 | 0,46 | 0,05 |
| | 44,13 | 0,93 | 0,41 | | |
| | 44,13 | 1,14 | 0,50 | | |
| DMNM 3 | 43,34 | 0,99 | 0,43 | 0,44 | 0,04 |
| | 43,34 | 0,95 | 0,41 | | |
| | 43,34 | 1,13 | 0,49 | | |

**Tabel 21. Kandungan metformin teoritis**

| Formula | Jumlah metformin (mg) | Rata-rata | Jumlah metformin (µg) | Rata-rata |
|---|---|---|---|---|
| DMNM1 | 0,094 | 0,095 | 94 | 95,49 |
| | 0,086 | | 86 | |
| | 0,105 | | 105 | |
| DMNM2 | 0,092 | 0,094 | 92 | 94,30 |
| | 0,085 | | 85 | |
| | 0,105 | | 105 | |
| DMNM3 | 0,090 | 0,093 | 90 | 93,13 |
| | 0,086 | | 86 | |
| | 0,103 | | 103 | |

**a. Contoh perhintungan jumlah mikropartikel metformin dalam *needle***

Diketahui :

Mikropartikel dalam massa kering DMNM2 replikasi 1 = 44,13

Bobot needle kering DMNM2 = 0,99

Jumlah *needle* DMN = 100

Rumus yang digunakan :

Jumlah mikropartikel metformin = $\frac{mikropartikel\ dalam\ massa\ kering}{jumlah\ needle\ DMN}$ x bobot *needle* kering

Sehingga

Jumlah mikropartikel metformin = $\frac{44,13}{100}$ x 0,99

= 0,44 mg

**c. Contoh perhitungan metformin teoritis**

Diketahui :

*Drug loading* metformin dalam mikropartikel = 20,93%

Bobot mikropartikel di jarum DMNM2 replikasi 1= 0,44mg

Jumlah metformin dalam formula = bobot mikropartikel di jarum x drug loading metformin dalam mikropartikel

= 0,44 x 20,93%

= 0,092mg

**c. Contoh perhitungan kandungan metformin dalam 100 *needle***

Diketahui :

Persamaan kurva baku di media PBS : y= 0,063x + 0,0425

Absorbansi replikasi 1 DMNM2 = 0,509

Konsentrasi metformin teoritis = 0,092mg

Persamaan yang digunakan

Konsentrasi metformin $= \frac{absorbansi - 0{,}0425}{0{,}063}$

Konsentrasi metformin $= \frac{0{,}509 - 0{,}0425}{0{,}063}$

= 7,40 µg/mL atau 74,05 µg/10mL

## Lampiran 7. Hasil Uji Permeasi *Ex Vivo*

**Tabel 22. Jumlah MTF yang berhasil terpermeasi di media PBS**

| Waktu (Jam) | replikasi | Absorbansi | Konsentrasi (µg/ml) | 0,5 ml (µg) | 8 ml (µg) | Faktor koreksi | Jumlah terpermeasi | Rata-rata | SD |
|---|---|---|---|---|---|---|---|---|---|
| 0,25 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 0,5 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 0,75 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 1 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 2 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 3 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 4 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 5 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 6 | 1 | 0 | -0,67 | -0,67 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | -0,67 | -0,67 | 0 | 0 | 0 | | |
| | 3 | 0 | -0,67 | -0,67 | 0 | 0 | 0 | | |
| 7 | 1 | 0,054 | 0,18 | 0,18 | 1,46 | -0,67 | 0,78 | 0,95 | 0,65 |
| | 2 | 0,061 | 0,29 | 0,29 | 2,35 | -0,67 | 1,67 | | |
| | 3 | 0,051 | 0,13 | 0,13 | 1,08 | -0,67 | 0,40 | | |
| 8 | 1 | 0,08 | 0,60 | 0,60 | 4,76 | -0,49 | 4,27 | 3,87 | 1,36 |
| | 2 | 0,064 | 0,34 | 0,34 | 2,73 | -0,38 | 2,35 | | |
| | 3 | 0,086 | 0,69 | 0,69 | 5,52 | -0,54 | 4,98 | | |
| 24 | 1 | 0,096 | 0,85 | 0,85 | 6,79 | 0,10 | 6,89 | 6,82 | 0,23 |
| | 2 | 0,098 | 0,88 | 0,88 | 7,05 | -0,04 | 7,00 | | |
| | 3 | 0,093 | 0,80 | 0,80 | 6,41 | 0,15 | 6,56 | | |

**Tabel 23. Jumlah MTF yang berhasil terpermeasi di media PBS + glukosa 1%**

| Waktu (Jam) | replikasi | Absorbansi | Konsentrasi (µg/ml) | 0,5 ml (µg) | 8 ml (µg) | Faktor koreksi | Jumlah terpermeasi | Rata-rata | SD |
|---|---|---|---|---|---|---|---|---|---|
| 0,25 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 0,5 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 0,75 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 1 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 2 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 3 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 4 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 5 | 1 | 0,051 | 0,13 | 0,13 | 1,08 | 0 | 1,08 | 2,81 | 1,61 |
| | 2 | 0,076 | 0,53 | 0,53 | 4,25 | 0 | 4,25 | | |
| | 3 | 0,067 | 0,39 | 0,39 | 3,11 | 0 | 3,11 | | |
| 6 | 1 | 0,09 | 0,75 | 0,75 | 6,03 | 0,13 | 6,17 | 7,65 | 1,32 |
| | 2 | 0,102 | 0,94 | 0,94 | 7,55 | 0,53 | 8,09 | | |
| | 3 | 0,108 | 1,04 | 1,04 | 8,32 | 0,39 | 8,71 | | |
| 7 | 1 | 0,121 | 1,25 | 1,25 | 9,97 | 0,89 | 10,86 | 10,51 | 0,42 |
| | 2 | 0,11 | 1,07 | 1,07 | 8,57 | 1,48 | 10,05 | | |
| | 3 | 0,115 | 1,15 | 1,15 | 9,21 | 1,43 | 10,63 | | |
| 8 | 1 | 0,132 | 1,42 | 1,42 | 11,36 | 2,13 | 13,5 | 13,53 | 1,16 |
| | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 24 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 21,14 | 1,62 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |

**Tabel 24. Jumlah MTF yang berhasil terpermeasi di media PBS + glukosa 2%**

| Waktu (Jam) | replikasi | Absorbansi | Konsentrasi (µg/ml) | 0,5 ml (µg) | 8 ml (µg) | Faktor koreksi | Jumlah terpermeasi | Rata-rata | SD |
|---|---|---|---|---|---|---|---|---|---|
| 0,25 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 0,5 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 0,75 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 1 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 2 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 3 | 1 | 0,054 | 0,18 | 0,18 | 1,46 | 0 | 1,46 | 1,12 | 0,39 |
| | 2 | 0,048 | 0,09 | 0,09 | 0,69 | 0 | 0,69 | | |
| | 3 | 0,052 | 0,15 | 0,15 | 1,21 | 0 | 1,21 | | |
| 4 | 1 | 0,087 | 0,71 | 0,71 | 5,65 | 0,18 | 5,83 | 5,45 | 0,98 |
| | 2 | 0,076 | 0,53 | 0,53 | 4,25 | 0,09 | 4,34 | | |
| | 3 | 0,09 | 0,75 | 0,75 | 6,03 | 0,15 | 6,18 | | |
| 5 | 1 | 0,1 | 0,91 | 0,91 | 7,30 | 0,89 | 8,19 | 8,44 | 0,66 |
| | 2 | 0,11 | 1,07 | 1,07 | 8,57 | 0,62 | 9,19 | | |
| | 3 | 0,098 | 0,88 | 0,88 | 7,05 | 0,90 | 7,95 | | |
| 6 | 1 | 0,121 | 1,25 | 1,25 | 9,97 | 1,80 | 11,77 | 11,85 | 0,62 |
| | 2 | 0,118 | 1,20 | 1,20 | 9,59 | 1,69 | 11,27 | | |
| | 3 | 0,127 | 1,34 | 1,34 | 10,73 | 1,78 | 12,51 | | |
| 7 | 1 | 0,125 | 1,31 | 1,31 | 10,48 | 3,05 | 13,52 | 13,83 | 0,57 |
| | 2 | 0,126 | 1,33 | 1,33 | 10,60 | 2,89 | 13,49 | | |
| | 3 | 0,132 | 1,42 | 1,42 | 11,36 | 3,13 | 14,49 | | |
| 8 | 1 | 0,142 | 1,58 | 1,58 | 12,63 | 4,36 | 16,99 | 17,81 | 2,01 |
| | 1 | 0,138 | 1,52 | 1,52 | 12,12 | 4,21 | 16,34 | | |
| | 2 | 0,165 | 1,94 | 1,94 | 15,56 | 4,55 | 20,10 | | |
| 24 | 3 | 0,232 | 3,01 | 3,01 | 24,06 | 5,94 | 30 | 33,63 | 3,78 |
| | 1 | 0,26 | 3,45 | 3,45 | 27,62 | 5,73 | 33,35 | | |
| | 2 | 0,287 | 3,88 | 3,88 | 31,05 | 6,49 | 37,54 | | |

**Tabel 25. Jumlah MTF yang berhasil terpermeasi di media PBS + glukosa 4%**

| Waktu (Jam) | replikasi | Absorbansi | Konsentrasi (µg/ml) | 0,5 ml (µg) | 8 ml (µg) | Faktor koreksi | Jumlah terpermeasi | Rata-rata | SD |
|---|---|---|---|---|---|---|---|---|---|
| 0,25 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 0,5 | 1 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | 0 | 0 |
| | 2 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| | 3 | 0 | 0,00 | 0,00 | 0 | 0 | 0 | | |
| 0,75 | 1 | 0,049 | 0,10 | 0,10 | 0,82 | 0 | 0,82 | 1,08 | 0,25 |
| | 2 | 0,053 | 0,17 | 0,17 | 1,33 | 0 | 1,33 | | |
| | 3 | 0,051 | 0,13 | 0,13 | 1,08 | 0 | 1,08 | | |
| 1 | 1 | 0,06 | 0,28 | 0,28 | 2,22 | 0,10 | 2,32 | 1,81 | 0,48 |
| | 2 | 0,052 | 0,15 | 0,15 | 1,21 | 0,17 | 1,37 | | |
| | 3 | 0,055 | 0,20 | 0,20 | 1,59 | 0,13 | 1,72 | | |
| 2 | 1 | 0,091 | 0,77 | 0,77 | 6,16 | 0,38 | 6,54 | 4,98 | 1,36 |
| | 2 | 0,072 | 0,47 | 0,47 | 3,71 | 0,32 | 4,06 | | |
| | 3 | 0,074 | 0,50 | 0,50 | 4 | 0,33 | 4,33 | | |
| 3 | 1 | 0,112 | 1,10 | 1,10 | 8,82 | 1,15 | 9,98 | 8,44 | 1,49 |
| | 2 | 0,102 | 0,94 | 0,94 | 7,56 | 0,78 | 8,34 | | |
| | 3 | 0,091 | 0,77 | 0,77 | 6,16 | 0,83 | 6,99 | | |
| 4 | 1 | 0,099 | 0,90 | 0,90 | 7,17 | 2,25 | 9,43 | 10,31 | 0,82 |
| | 2 | 0,111 | 1,09 | 1,09 | 8,69 | 1,73 | 10,43 | | |
| | 3 | 0,117 | 1,18 | 1,18 | 9,46 | 1,60 | 11,06 | | |
| 5 | 1 | 0,122 | 1,26 | 1,26 | 10,09 | 3,15 | 13,24 | 12,55 | 1,14 |
| | 2 | 0,124 | 1,29 | 1,29 | 10,35 | 2,82 | 13,16 | | |
| | 3 | 0,109 | 1,06 | 1,06 | 8,44 | 2,78 | 11,23 | | |
| 6 | 1 | 0,125 | 1,31 | 1,31 | 10,48 | 4,41 | 14,89 | 15,99 | 1,11 |
| | 2 | 0,136 | 1,48 | 1,48 | 11,87 | 4,11 | 15,98 | | |
| | 3 | 0,147 | 1,66 | 1,66 | 13,27 | 3,84 | 17,11 | | |
| 7 | 1 | 0,158 | 1,83 | 1,83 | 14,67 | 5,72 | 20,39 | 21,79 | 1,34 |
| | 2 | 0,180 | 2,18 | 2,18 | 17,46 | 5,59 | 23,05 | | |
| | 3 | 0,172 | 2,06 | 2,06 | 16,44 | 5,50 | 21,94 | | |
| 8 | 1 | 0,191 | 2,36 | 2,36 | 18,86 | 7,55 | 26,41 | 27,92 | 1,46 |
| | 1 | 0,202 | 2,53 | 2,53 | 20,25 | 7,77 | 28,03 | | |
| | 2 | 0,214 | 2,72 | 2,72 | 21,78 | 7,55 | 29,33 | | |
| 24 | 3 | 0,347 | 4,83 | 4,83 | 38,67 | 9,91 | 48,58 | 51,41 | 3,00 |
| | 1 | 0,391 | 5,53 | 5,53 | 44,25 | 10,31 | 54,56 | | |
| | 2 | 0,364 | 5,10 | 5,10 | 40,82 | 10,28 | 51,10 | | |

## Lampiran 8. Data Analisis Statistika

## Lampiran 8.1 Evaluasi kekuatan mekanik *dissolving microneedle*

### Normalitas

Tabular results

Normality and Lognormality Tests
Tabular results

| | | A | B | C |
|---|---|---|---|---|
| | | DMNM1 | DMNM2 | DMNM3 |
| | | Y | Y | Y |
| 1 | **Test for normal distribution** | | | |
| 2 | **Shapiro-Wilk test** | | | |
| 3 | W | 0.9794 | 0.7785 | 0.9751 |
| 4 | P value | 0.7251 | 0.0641 | 0.6972 |
| 5 | Passed normality test (alpha=0.05)? | Yes | Yes | Yes |
| 6 | P value summary | ns | ns | ns |
| 7 | | | | |
| 8 | **Number of values** | 3 | 3 | 3 |

### ANOVA

ANOVA results | Multiple comparisons

Ordinary one-way ANOVA
ANOVA results

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | Table Analyzed | Kekuatan mekanik | | | | |
| 2 | Data sets analyzed | A-C | | | | |
| 3 | | | | | | |
| 4 | **ANOVA summary** | | | | | |
| 5 | F | 62.02 | | | | |
| 6 | P value | <0.0001 | | | | |
| 7 | P value summary | **** | | | | |
| 8 | Significant diff. among means (P < 0.05)? | Yes | | | | |
| 9 | R squared | 0.9539 | | | | |
| 10 | | | | | | |
| 11 | **Brown-Forsythe test** | | | | | |
| 12 | F (DFn, DFd) | | | | | |
| 13 | P value | | | | | |
| 14 | P value summary | | | | | |
| 15 | Are SDs significantly different (P < 0.05)? | | | | | |
| 16 | | | | | | |
| 17 | **Bartlett's test** | | | | | |
| 18 | Bartlett's statistic (corrected) | | | | | |
| 19 | P value | | | | | |
| 20 | P value summary | | | | | |
| 21 | Are SDs significantly different (P < 0.05)? | | | | | |
| 22 | | | | | | |
| 23 | **ANOVA table** | **SS** | **DF** | **MS** | **F (DFn, DFd)** | **P value** |
| 24 | Treatment (between columns) | 575.2 | 2 | 287.6 | F (2, 6) = 62.02 | P<0.0001 |
| 25 | Residual (within columns) | 27.82 | 6 | 4.637 | | |
| 26 | Total | 603.0 | 8 | | | |
| 27 | | | | | | |

## Multiple Comparison

ANOVA results | Multiple comparisons

Ordinary one-way ANOVA
Multiple comparisons

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Number of families | 1 | | | | | | | |
| 2 | Number of comparisons per family | 3 | | | | | | | |
| 3 | Alpha | 0.05 | | | | | | | |
| 4 | | | | | | | | | |
| 5 | **Tukey's multiple comparisons test** | **Mean Diff.** | **95.00% CI of diff.** | **Below threshold?** | **Summary** | **Adjusted P Value** | | | |
| 6 | DMNM1 vs. DMNM2 | 14.88 | 9.486 to 20.27 | Yes | *** | 0.0004 | A-B | | |
| 7 | DMNM1 vs. DMNM3 | 18.46 | 13.07 to 23.86 | Yes | *** | 0.0001 | A-C | | |
| 8 | DMNM2 vs. DMNM3 | 3.583 | -1.811 to 8.978 | No | ns | 0.1839 | B-C | | |
| 9 | | | | | | | | | |
| 10 | **Test details** | **Mean 1** | **Mean 2** | **Mean Diff.** | **SE of diff.** | **n1** | **n2** | **q** | **DF** |
| 11 | DMNM1 vs. DMNM2 | 24.52 | 9.643 | 14.88 | 1.758 | 3 | 3 | 11.97 | 6 |
| 12 | DMNM1 vs. DMNM3 | 24.52 | 6.060 | 18.46 | 1.758 | 3 | 3 | 14.85 | 6 |
| 13 | DMNM2 vs. DMNM3 | 9.643 | 6.060 | 3.583 | 1.758 | 3 | 3 | 2.882 | 6 |
| 14 | | | | | | | | | |
| 15 | | | | | | | | | |

## Lampiran 8.2 Uji kemampuan penetrasi *dissolving microneedle*

## Normalitas

Tabular results

| Normality and Lognormality Tests<br>Tabular results | | A | B |
|---|---|---|---|
| | | DMNM2 | DMNM3 |
| | | Y | Y |
| 1 | **Test for normal distribution** | | |
| 2 | **Shapiro-Wilk test** | | |
| 3 | W | 0.9959 | 0.9868 |
| 4 | P value | 0.8776 | 0.7804 |
| 5 | Passed normality test (alpha=0.05)? | Yes | Yes |
| 6 | P value summary | ns | ns |
| 7 | | | |
| 8 | **Number of values** | 3 | 3 |
| 9 | | | |
| 10 | | | |
| 11 | | | |

## T-test

Tabular results

| | Unpaired t test<br>Tabular results | |
|---|---|---|
| 1 | Table Analyzed | kemampuan penetrasi normalitas |
| 2 | | |
| 3 | Column B | DMNM3 |
| 4 | vs. | vs. |
| 5 | Column A | DMNM2 |
| 6 | | |
| 7 | **Unpaired t test** | |
| 8 | P value | 0.0004 |
| 9 | P value summary | *** |
| 10 | Significantly different (P < 0.05)? | Yes |
| 11 | One- or two-tailed P value? | Two-tailed |
| 12 | t, df | t=11.04, df=4 |
| 13 | | |
| 14 | **How big is the difference?** | |
| 15 | Mean of column A | 76.33 |
| 16 | Mean of column B | 16.67 |
| 17 | Difference between means (B - A) ± SEM | -59.67 ± 5.406 |
| 18 | 95% confidence interval | -74.68 to -44.66 |
| 19 | R squared (eta squared) | 0.9682 |
| 20 | | |
| 21 | **F test to compare variances** | |
| 22 | F, DFn, Dfd | 12.84, 2, 2 |
| 23 | P value | 0.1445 |
| 24 | P value summary | ns |
| 25 | Significantly different (P < 0.05)? | No |
| 26 | | |
| 27 | **Data analyzed** | |

## Lampiran 8.3 Uji permease *ex vivo*

## Normalitas

Tabular results

| Normality and Lognormality Tests<br>Tabular results | A<br>Media PBS | B<br>Media PBS + Glukosa 1% | C<br>Media PBS + Glukosa 2% | D<br>Media PBS + Glukosa 4% | E<br>Title |
|---|---|---|---|---|---|
| | Y | Y | Y | Y | Y |
| **Test for normal distribution** | | | | | |
| **Shapiro-Wilk test** | | | | | |
| W | 0.9231 | 0.9954 | 0.9959 | 0.9919 | |
| P value | 0.4633 | 0.8705 | 0.8771 | 0.8279 | |
| Passed normality test (alpha=0.05)? | Yes | Yes | Yes | Yes | |
| P value summary | ns | ns | ns | ns | |
| | | | | | |
| **Number of values** | 3 | 3 | 3 | 3 | |

## ANOVA

ANOVA results | Multiple comparisons

| Ordinary one-way ANOVA<br>ANOVA results | | | | | |
|---|---|---|---|---|---|
| Table Analyzed | Permeasi ex-vivo anova | | | | |
| Data sets analyzed | A-D | | | | |
| | | | | | |
| **ANOVA summary** | | | | | |
| F | 162.6 | | | | |
| P value | <0.0001 | | | | |
| P value summary | **** | | | | |
| Significant diff. among means (P < 0.05)? | Yes | | | | |
| R squared | 0.9839 | | | | |
| | | | | | |
| **Brown-Forsythe test** | | | | | |
| F (DFn, DFd) | | | | | |
| P value | | | | | |
| P value summary | | | | | |
| Are SDs significantly different (P < 0.05)? | | | | | |
| | | | | | |
| **Bartlett's test** | | | | | |
| Bartlett's statistic (corrected) | | | | | |
| P value | | | | | |
| P value summary | | | | | |
| Are SDs significantly different (P < 0.05)? | | | | | |
| | | | | | |
| **ANOVA table** | **SS** | **DF** | **MS** | **F (DFn, DFd)** | **P value** |
| Treatment (between columns) | 3168 | 3 | 1056 | F (3, 8) = 162. | P<0.0001 |
| Residual (within columns) | 51.97 | 8 | 6.496 | | |
| Total | 3220 | 11 | | | |

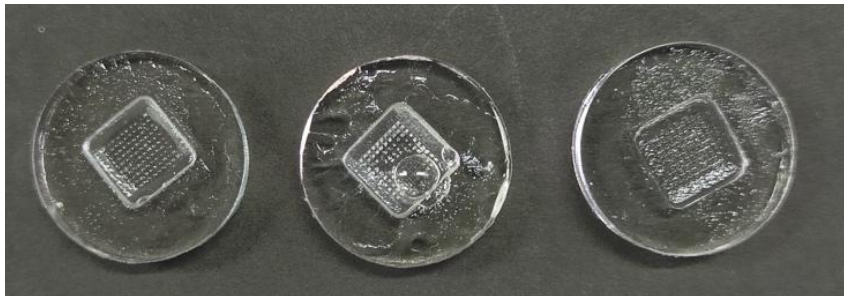
## Multiple Comparison

ANOVA results | Multiple comparisons

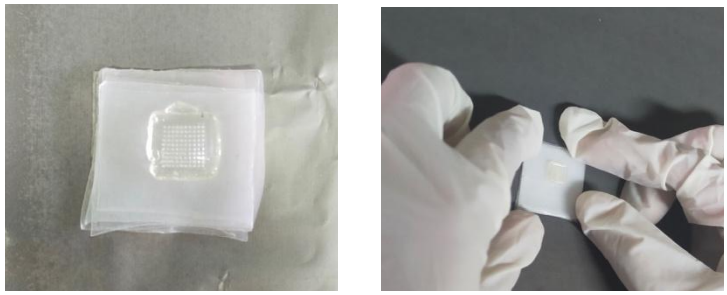
Ordinary one-way ANOVA
Multiple comparisons

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Number of families | 1 | | | | | | | |
| 2 | Number of comparisons per family | 6 | | | | | | | |
| 3 | Alpha | 0.05 | | | | | | | |
| 4 | | | | | | | | | |
| 5 | **Tukey's multiple comparisons test** | **Mean Diff.** | **95.00% CI of diff.** | **Below threshold?** | **Summary** | **Adjusted P Value** | | | |
| 6 | Media PBS vs. Media PBS + Glukosa 1% | -14.32 | -20.98 to -7.656 | Yes | *** | 0.0006 | A-B | | |
| 7 | Media PBS vs. Media PBS + Glukosa 2% | -26.81 | -33.47 to -20.14 | Yes | **** | <0.0001 | A-C | | |
| 8 | Media PBS vs. Media PBS + Glukosa 4% | -44.18 | -50.84 to -37.51 | Yes | **** | <0.0001 | A-D | | |
| 9 | Media PBS + Glukosa 1% vs. Media PBS + Glukosa 2% | -12.49 | -19.15 to -5.823 | Yes | ** | 0.0015 | B-C | | |
| 10 | Media PBS + Glukosa 1% vs. Media PBS + Glukosa 4% | -29.86 | -36.52 to -23.19 | Yes | **** | <0.0001 | B-D | | |
| 11 | Media PBS + Glukosa 2% vs. Media PBS + Glukosa 4% | -17.37 | -24.03 to -10.71 | Yes | *** | 0.0001 | C-D | | |
| 12 | | | | | | | | | |
| 13 | **Test details** | **Mean 1** | **Mean 2** | **Mean Diff.** | **SE of diff.** | **n1** | **n2** | **q** | **DF** |
| 14 | Media PBS vs. Media PBS + Glukosa 1% | 6.823 | 21.14 | -14.32 | 2.081 | 3 | 3 | 9.732 | 8 |
| 15 | Media PBS vs. Media PBS + Glukosa 2% | 6.823 | 33.63 | -26.81 | 2.081 | 3 | 3 | 18.22 | 8 |
| 16 | Media PBS vs. Media PBS + Glukosa 4% | 6.823 | 51.00 | -44.18 | 2.081 | 3 | 3 | 30.02 | 8 |
| 17 | Media PBS + Glukosa 1% vs. Media PBS + Glukosa 2% | 21.14 | 33.63 | -12.49 | 2.081 | 3 | 3 | 8.486 | 8 |
| 18 | Media PBS + Glukosa 1% vs. Media PBS + Glukosa 4% | 21.14 | 51.00 | -29.86 | 2.081 | 3 | 3 | 20.29 | 8 |
| 19 | Media PBS + Glukosa 2% vs. Media PBS + Glukosa 4% | 33.63 | 51.00 | -17.37 | 2.081 | 3 | 3 | 11.80 | 8 |
| 20 | | | | | | | | | |
| 21 | | | | | | | | | |

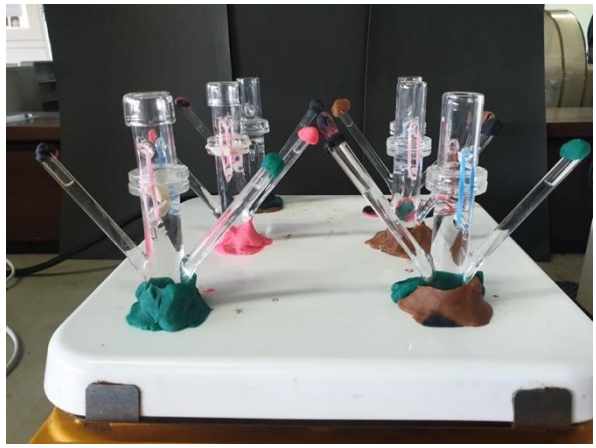
## Lampiran 9. Gambar Penelitian



**Gambar 16. Formula DMNM masuk ke dalam cetakan**



**Gambar 17. Evaluasi kekuatan mekanik dan kemampuan penetrasi DMNM**



**Gambar 18. Uji permeasi *ex vivo* dalam media PBS, PBS+glukosa 1%, PBS+glukosa 2%, dan PBS+glukosa 4%,**