

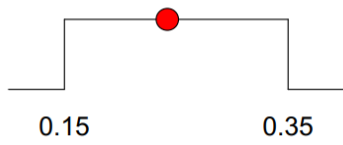
Appendix 1. Result of ANOVA for Response Surface Reduced Cubic Model (Analysis of variance table [Partial sum of squares - Type III])

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	1958.29	10	195.83	2243.38	< 0.0001	significant
<i>C-PEG</i>	<i>739.84</i>	<i>1</i>	<i>739.84</i>	<i>8475.49</i>	<i>< 0.0001</i>	
<i>AB</i>	<i>19.80</i>	<i>1</i>	<i>19.80</i>	<i>226.85</i>	<i>0.0001</i>	
<i>AC</i>	<i>336.72</i>	<i>1</i>	<i>336.72</i>	<i>3857.44</i>	<i>< 0.0001</i>	
<i>BC</i>	<i>65.61</i>	<i>1</i>	<i>65.61</i>	<i>751.62</i>	<i>< 0.0001</i>	
<i>A²</i>	<i>2.56</i>	<i>1</i>	<i>2.56</i>	<i>29.37</i>	<i>0.0056</i>	
<i>B²</i>	<i>351.60</i>	<i>1</i>	<i>351.60</i>	<i>4027.88</i>	<i>< 0.0001</i>	
<i>C²</i>	<i>173.67</i>	<i>1</i>	<i>173.67</i>	<i>1989.58</i>	<i>< 0.0001</i>	
<i>A²B</i>	<i>138.06</i>	<i>1</i>	<i>138.06</i>	<i>1581.62</i>	<i>< 0.0001</i>	
<i>A²C</i>	<i>168.36</i>	<i>1</i>	<i>168.36</i>	<i>1928.72</i>	<i>< 0.0001</i>	
<i>AB²</i>	<i>89.30</i>	<i>1</i>	<i>89.30</i>	<i>1023.04</i>	<i>< 0.0001</i>	
Residual	0.35	4	0.087			
<i>Lack of Fit</i>	<i>2.500E-003</i>	<i>2</i>	<i>1.250E-003</i>	<i>7.212E-003</i>	<i>0.9928</i>	<i>not significant</i>
<i>Pure Error</i>	<i>0.35</i>	<i>2</i>	<i>0.17</i>			
Cor Total	1958.64	14				

Appendix 2. The result of PMNs insetion test.

Formulatin	Test No	Total	Layer 1		Layer 2		Layer 3		Layer 4		Layer 5	
			N*	PR**	N	PR	N	PR	N	PR	N	PR
FO	1	121.0	121.0	100.0	121.0	100.0	121.0	100.0	68.0	56.2	3.0	2.5
	2	121.0	121.0	100.0	121.0	100.0	121.0	100.0	73.0	60.3	5.0	4.1
	3	121.0	121.0	100.0	121.0	100.0	121.0	100.0	79.0	65.3	7.0	5.8
	Mean	121.0	121.0	100.0	121.0	100.0	121.0	100.0	73.3	60.6	5.0	4.1
	SD	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.5	4.6	2.0	1.7

* number of microneedle **Penetration rate



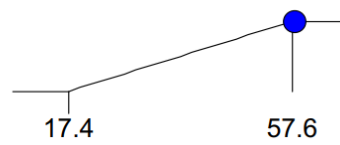
CMC = 0.24



HA = 0.09

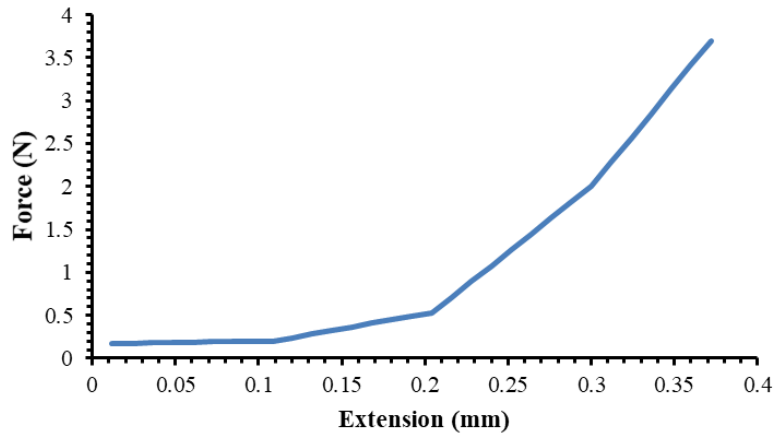


PEG = 0.50

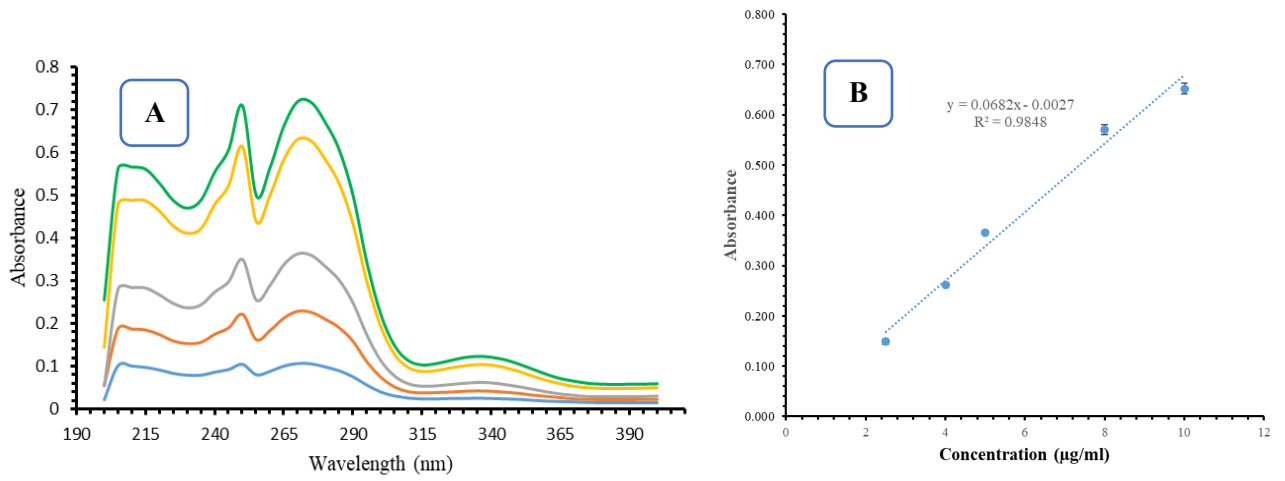


R = 58.1938

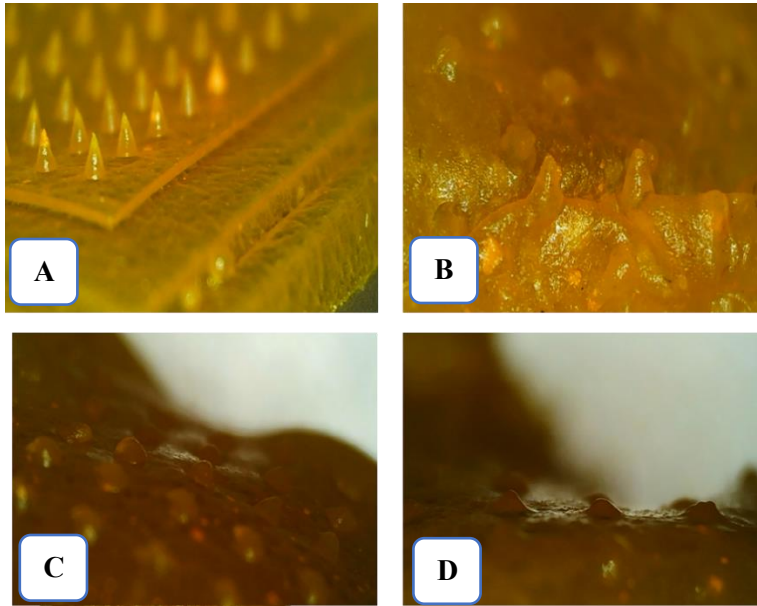
Appendix 3. The quantity of optimized factors for the proposed formulation and the predicted release percentage for it.



Appendix 4. Compression (force vs. displacement) diagram of the PMNs



Appendix 5. A: Lawson absorption within the range of 200 to 400 nm; B: Standard calibration curve for determining Lawson concentration.



Appendix 6. Image of PMNs following exposure to the gelatin block at time A: zero, B: one, C: three, and D: five minutes