Supplementary Information

A Microneedle Transdermal Patch loaded with Iron(II) Nanoparticles for Non-invasive Sustained Delivery to Combat Anemia

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Table S1. Some of the tested compositions for preparation of polymeric films containing IS NPs (each experiment repeated in triplicate).

S. No.	Batch Name	IS NPs (mg)	PLGA (mg)	PEG (mg)	PVA (mg)	ACN (ml)	Drug Release on day 1[#], % (averaged)
1	50IS-PLGA25	18.4 (40%)	46 (100%), 25 KDa	-	-	1	2%*
2	50IS-PEG2	18.4 (40%)	-	46 (100%), 2 KDa	-	1	94%
3	50IS-30PLGA25-PEG2	18.4 (40%)	13.8 (30%), 25 KDa	32.2 (70%), 2 KDa	-	1	62%
4	50IS-70PLGA25-PEG2	18.4 (40%)	32.2 (70%), 25 KDa	13.8 (30%), 2 KDa	-	1	60%
5	30IS-80PLGA25-PVA	13.8 (30%)	36.8 (80%), 25 KDa	-	9.2 (20%)	1	47%
6	50IS-70PLGA25-PVA	18.4 (40%)	32.2 (70%), 25 KDa	-	13.8 (30%)	1	61%
7	50IS-80PLGA25-PVA	18.4 (40%)	36.8 (80%), 25 KDa	-	9.2 (20%)	1	60%
8	50IS-90PLGA25-PVA	18.4 (40%)	41.4 (90%), 25 KDa	-	4.6 (10%)	1	74%
9	30IS-30PLGA25-PEG2	13.8 (30%)	13.8 (30%), 25 KDa	32.2 (70%), 2 KDa	-	1	79%

10	50IS-30PLGA25-PEG2-5	36.8 (40%)	27.6 (30%), 25 KDa	64.4 (70%), 2 KDa	-	2	84%
11	50IS-50PLGA25-PEG2	18.4 (40%)	23 (50%), 25 KDa	23 (50%), 2 KDa	-	1	83%
12	50IS-50PLGA25-PEG6	18.4 (40%)	23 (50%), 25 KDa	23 (50%), 6 KDa	-	1	77%
13	50IS-50PLGA25-PEG20	18.4 (40%)	23 (50%), 25 KDa	23 (50%), 20 KDa	-	1	66%
14	50IS-PEG20	18.4 (40%)	-	46 (100%), 20 KDa	-	1	87%
15	30IS-30PLGA120-PEG2	13.8 (30%)	13.8 (30%) (50:50) 120 KDa	32.2 (70%), 2KDa	-	1	86%
16	30IS-30PLGA60-PEG2	13.8 (30%)	13.8 (30%) (75:25) 60 KDa	32.2 (70%), 2KDa	-	1	89%
17	30IS-30PLGA160-PEG2	13.8 (30%)	13.8 (30%) (75:25) 160 KDa	32.2 (70%), 2KDa	-	1	88%
18	30IS-30PLGA60-PEG2-1	13.8 (30%)	13.8 (30%) (50:50) 60 KDa	32.2 (70%) 2 KDa	-	1	88%
19	15IS-90PLGA60-PEG2	6.9 (15%)	41.4 (90%) (50:50) 60 KDa	4.6 (10%) 2 KDa	-	1	2%**
20	30IS-80PLGA60-PEG2	13.8 (30%)	36.8 (80%) (50:50) 60 KDa	9.2 (20%) 2KDa	-	1	4%***
21	30IS-70PLGA60-PEG2-3	13.8 (30%)	32.2 (70%) (50:50) 60 KDa	13.8 (30%) 2KDa	-	1	13%
22	30IS-70PLGA60-PEG10-4	13.8 (30%)	32.2 (70%) (50:50) 60 KDa	13.8 (30%) 10KDa	-	1	60%
23	30IS-70PLGA60-PEG10-5	13.8 (30%)	32.2 (70%) (50:50) 60 KDa	13.8 (30%) 10KDa	-	1	58%
24	5IS-70PLGA60-PEG10	2.3 (5%)	32.2 (70%) (50:50) 60 KDa	13.8 (30%) 10KDa	-	1	18%
25	10IS-70PLGA60-PEG10	4.6 (10%)	32.2 (70%) (50:50) 60 KDa	13.8 (30%) 10KDa	-	1	44%

26	20IS-70PLGA60-PEG10	9.2 (20%)	32.2 (70%) (50:50) 60 KDa	13.8 (30%) 10KDa	-	1	45%
27	**30IS-70PLGA60-PEG10**	**13.8 (30%)**	**32.2 (70%) (50:50) 60 KDa**	**13.8 (30%) 10KDa**	**-**	**1**	**26% - Selected as the best formulation**
28	40IS-70PLGA60-PEG10	18.4 (40%)	32.2 (70%) (50:50) 60 KDa	13.8 (30%) 10KDa	-	1	61%
29	30IS-70PLGA60-PEG10	13.8 (30% - bulk IS, not NPs)	32.2 (70%) (50:50) 60 KDa	13.8 (30%) 10KDa	-	1	58%

94-97 % of total loaded drug was released on day 14
* only 31% of total loaded drug was released on day 7
** only 32% of total loaded drug was released on day 7
*** only 35% of total loaded drug was released on day 7

The remaining 33 compositions were excluded from Table S1 as they either did not demonstrate any improvement in burst release control or lacked consistency in daily drug release. For clarity, here is a breakdown of the excluded compositions:

1. 20% of PLGA (50:50), 25 kDa, 60 kDa, 120 kDa, 160 kDa mixed with 80% of PEG 2kDa, 6 kDa, and 10 kDa each + 30% IS – 12 compositions;
2. 40% of PLGA (50:50), 25 kDa, 60 kDa, 120 kDa, 160 kDa mixed with 80% of PEG 2kDa, 6 kDa, and 10 kDa each + 30% IS – 12 compositions;
3. 60% of PLGA (50:50), 25 kDa, 60 kDa, 160 kDa mixed with 80% of PEG 2kDa, 6 kDa, and 10 kDa each + 30% IS – 9 compositions.

Additionally, attempts were made to combine PLGA 60 kDa + PEG 2 and 10 kDa with Hyaluronic Acid and Polyvinylpyrrolidone (PVP). Unfortunately, these four compositions did not result in a uniformly mixed matrix and exhibited very uneven drug release (30% IS was used).

Table S2. Summary of the tested polymeric compositions with color-coded results for the evaluated parameters.

Polymer Type →	No PEG/PVA	PEG 2 kDa	PEG 6 kDa	PEG 10 kDa	PEG 20 kDa	PVA
No PLGA		X X X			X X	
PLGA 25 kDa	X	X	X X		X X	X X X
PLGA 60 kDa		X		√		
PLGA 120 kDa		X X				
PLGA 160 kDa		X X				

√ - all parameters are up to expectation
X – one of the parameters is not up to expectation
XX - two parameters are not up to expectation
XXX – all three parameters are not up to expectation

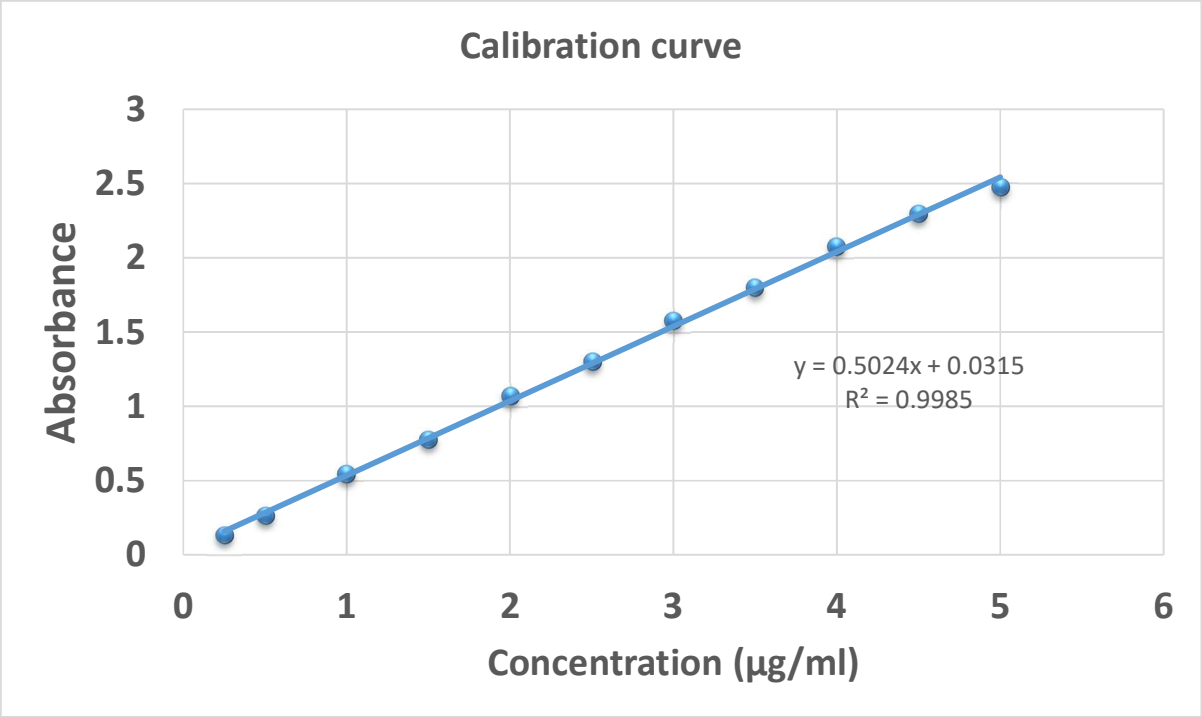

Figure S1. The calibration curve for Iron quantification in formulation, developed using Spectroquant Iron Test Kit.

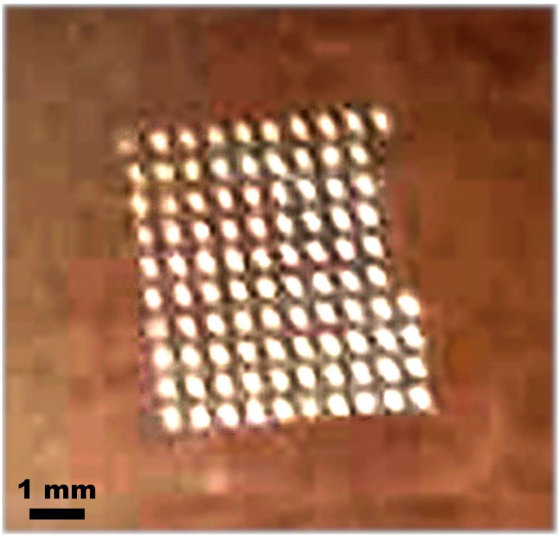

Figure S2. Optical microscope image shows artificial skin model after piercing with MNs (MNs patch applied for 5 seconds and removed)

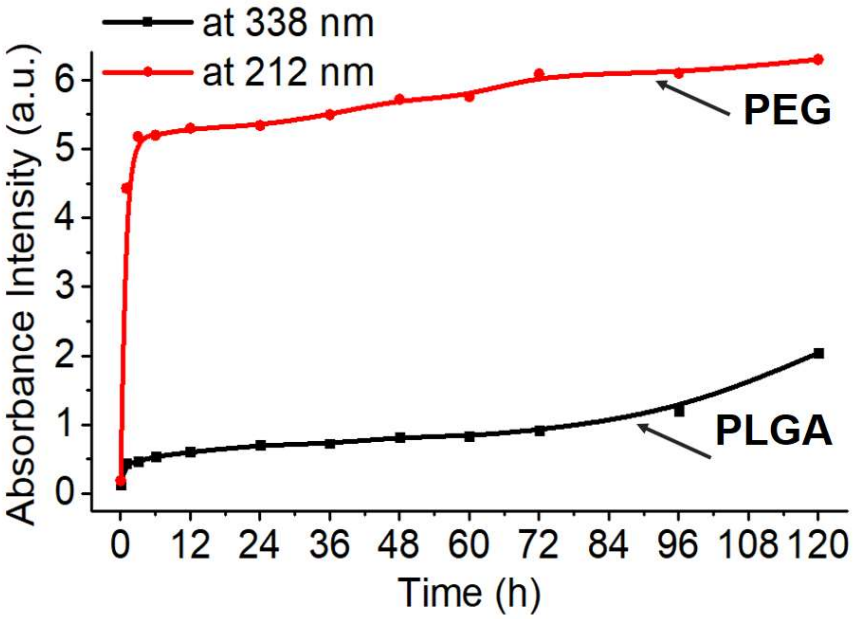

Figure S3. Normalized absorbance spectra versus time for the MNs samples immersed in water: demonstrating dissolution of the polymers (PLGA –black line, and PEG – red line). The measurements were done at the following time points: 0, 1h, 3h, 6h, 12h, 36h, 48h, 60h, 72h, 96h, 120h. Produced using UV-vis spectrophotometry (Eppendorf BioSpectrometer - Basic).

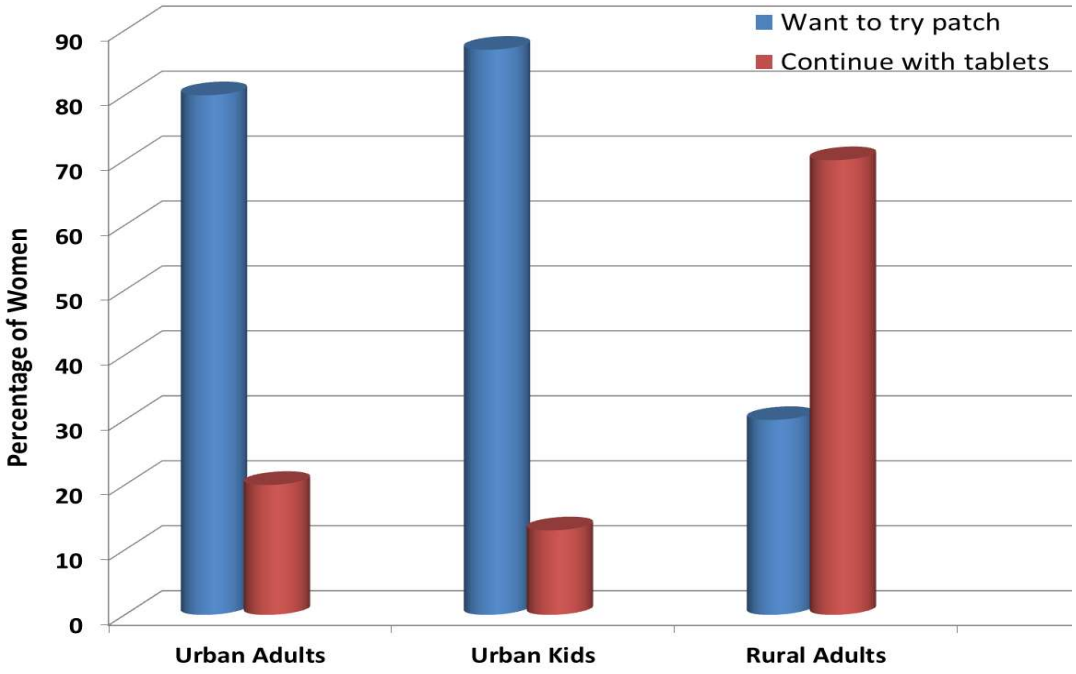

Figure S4. The results of the preliminary "Acceptance survey" conducted among potential end-users in urban and rural areas around Hyderabad.

Table S3. Acceptance Survey – Potential End Users.

Sl. No	Criteria	Agreed	Neutral	Disagreed
1	Supplements Critical Micronutrients	89.5%	10%	0.5%

2	Good addition to existing interventions	91.5%	8.5%	NIL
3	Delivers over extended time period	30.5%	51.5%	18%
4	Happy to use patch if it becomes available instead of other existing	63.2%	29.5%	6.3%
5	Apply on Self before applying on other family members + males	70.6%	19%	10.4%
6	Interference with my day to day activities	27.4%	32.6%	40%
7	Concerned that patch may be unaffordable compared to tablets/inj	36.7%	32.6%	30.7%
8	Want to see others using it before I use it	47.4%	24.2%	28.4%

Table S4. Acceptance Survey – Potential service providers.

Sl. No	Criteria	Agreed	Neutral	Disagreed
1	Supplements Critical Micronutrients	75%	13%	2%
2	Good addition to existing interventions	93%	6%	1%
3	Delivers over extended time period	55%	34%	11%
4	Better or equal to existing modalities	41%	36%	23%
5	Apply on Self before applying on others	78%	14%	8%

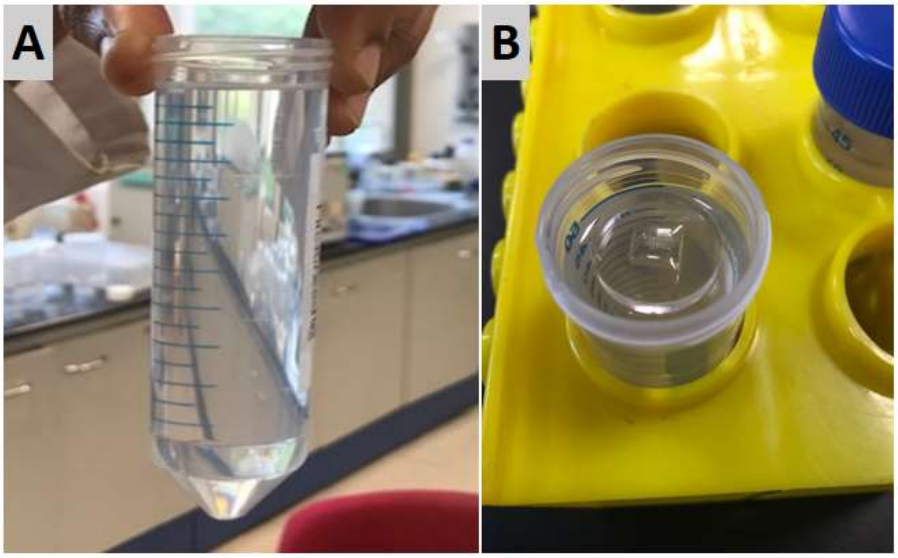

Figure S5. **A)** Falcon tube filled with PDMS used as a stand for MNs mold, and B) MNs template placed in the above stand.