Transdermal Delivery of Fluphenazine Decanoate Using Hybrid System of Nanoemulsion and Microneedles.

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Background:

As a chronic treatment of schizophrenia, fluphenazine decanoate (FLU-D) is administered intramuscularly every 2-4 weeks (1). Schizophrenia disease related to poor patient adherence due to the this disease requires lifelong treatment, even when patient has no symptoms. Therefore, to improve the clinical outcomes of antipsychotics, continues effort is directed toward investigating different dosage forms or routes of administration (2). Microneedles (MNs) has a promising ability to bypass the stratum corneum barrier, thus, enhancing the transdermal permeation (3). Nanoemulsion (NE) has been investigated previously as a nanocarrier of lipophilic molecules (4). NE improves the permeation of lipophilic compounds through the biological membranes (4). Combining various permeation enhancers such as NE and microneedle technology is potentially enhance molecules permeation through the skin (2).

Methods

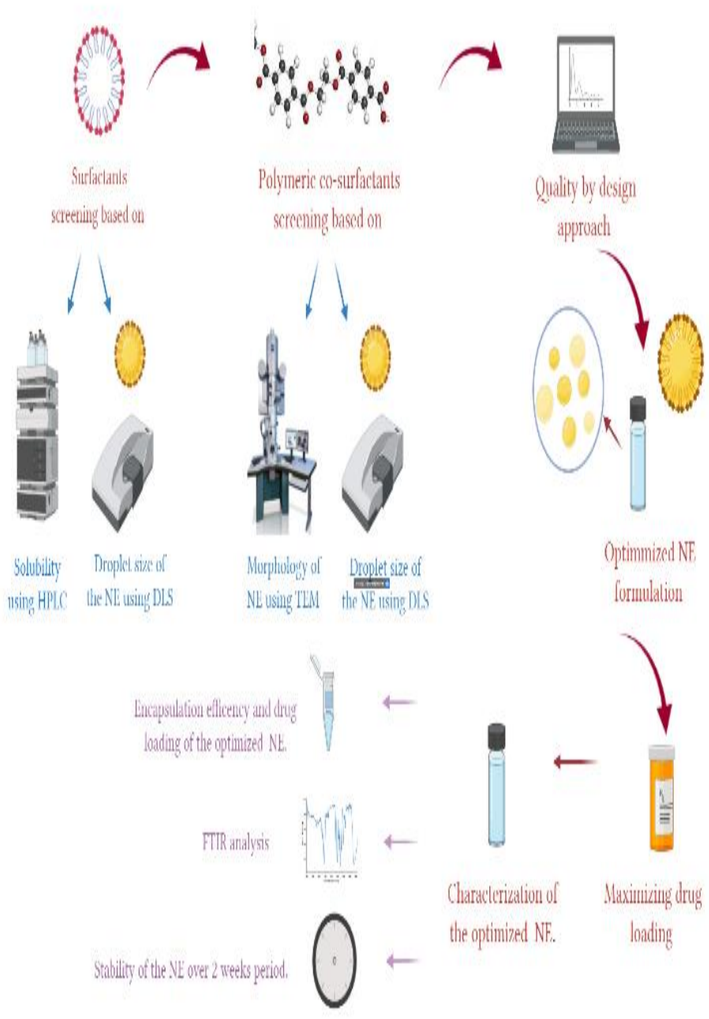


Figure1: Optimization method of FLU-D NE.

Results and Discussion

The optimised FLU-D NE properties are demonstrated in Table 1. FLU-D NE loaded dissolving MNs showed a sufficient mechanical and insertion properties to bypass the *stratum corneum* as shown in Figure 4. Both FLU-D and FLU were found to be deposited in the skin as shown in Figure 5. The *in situ* dissolution time of MNs loaded with FLU-D-NE was less than 10 mins as displayed in Figure 6.

FLU-D NE characterisation

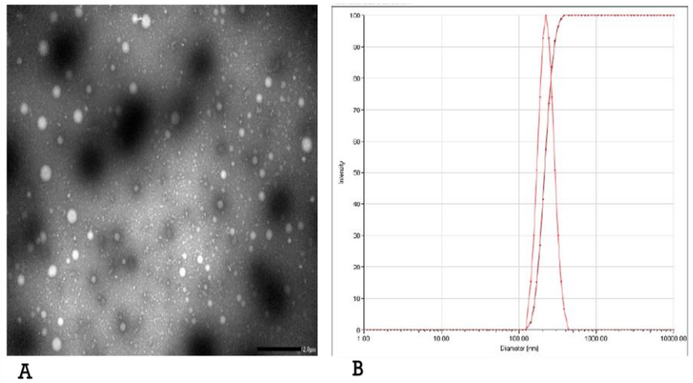


Figure 2: A) TEM image of the optimized FLU-D NE, B) DLS graph showing droplet size distribution of the optimized FLU-D NE.

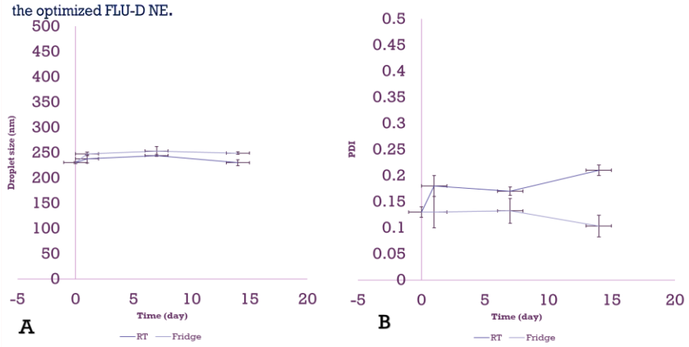
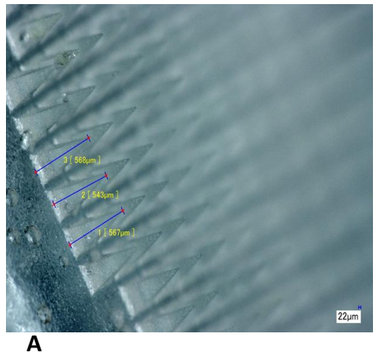


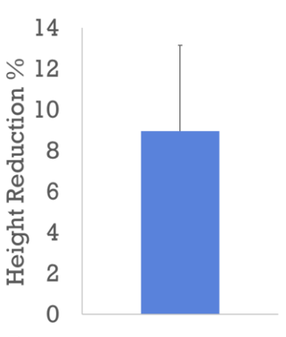
Figure 3: FLU-D NE stability in terms of A: droplet size, B: PDI over a period of 14 days

Table1: FLU-D NE characterization. Mean ±SD, n=3

Droplet size	210 ± 5 nm
PDI	0.14 ± 0.01
Encapsulation efficacy%	99.81 ±0.1%

Characterisation of MNs loaded with FLU-D NE





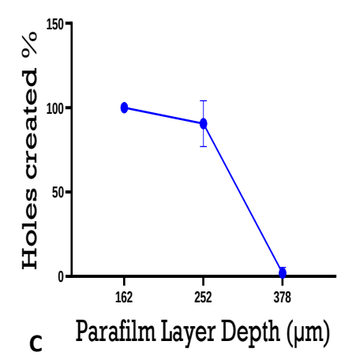


Figure 4: A) Microscopic image of MNs. B) Height reduction % after compression force test. C) Holes created % in parafilm M® following the insertion test (mean ± SD, n=3)

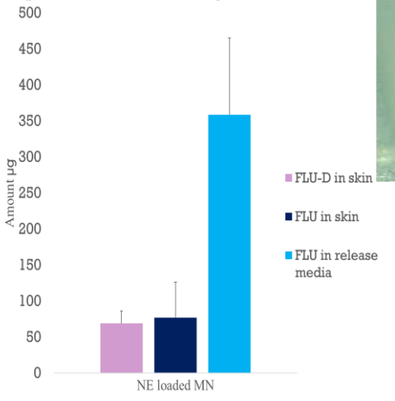


Figure 5: Amount (µg) of FLU and FLU-D deposited in the skin and release media after 24 hours of MNs insertion onto full thickness porcine skin (Mean± SD, n=5).

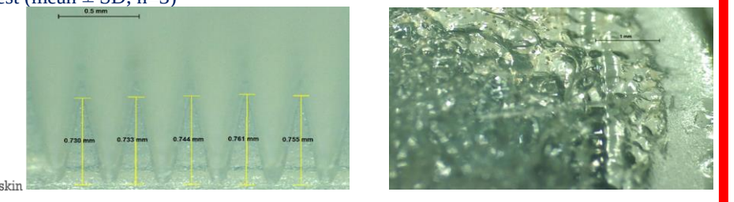


Figure 6: A) MNs length before in skin insertion. B) after 10m of MNs insertion to full thickness porcine skin

Conclusion

These findings suggest that this oily lipophilic prodrug can be delivered transdermally using this novel hybrid system of MNs and NE

References

1. (Stahl, 2008) 2. (Abruzzo, 2019)
3. (Donnelly and Larrañeta,2018) 4. (Attwood,2003)