NOVEL FLU-D NANOEMULSION LOADED DISSOLVING MICRONEEDLES ARRAY FOR TRANSDERMAL DELIVERY.

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Background: As a chronic treatment of schizophrenia, fluphenazine decanoate (FLU-D) is administered intramuscularly every 2- 4 week. Schizophrenia symptoms and Lack of illness insight boost poor medications adherence. To improve the clinical outcomes of antipsychotics, continues effort is directed toward investigating different dosage forms or routes of administration. Transdermal delivery as a self-administered dosage form has the potential to benefit the medical practice and enhance patients adherence to prescriptions. Nanoemulsion (NE) has been investigated previously as a nanocarrier of lipophilic molecules. NE improves the permeation of lipophilic compounds through the biological membranes. Further, Microneedles bypass the *stratum cornium* (SC) to enhance the transdermal permeation. Combining various permeation enhancers such as NE and MNs can enhance molecules permeation through the skin.

Methods: The FLU-D NE was prepared by sonication method. NE components were screened based on drug solubility, droplet size and polydispersity index (PDI) using HPLC, particle sizer and transmission electron microscopy (TEM) respectively. Further, a quality by design approach was applied to optimize FLU-D NE using Design-Expert® software. Finally, FLU-D NE was loaded to polymeric DMNs formulation to form bilayer DMNs. FLU-D NE loaded DMNs were characterized, and i*n-vitro* skin dissolution and deposition were studied in full-thickness neonatal porcine skin (obtained from stillborn piglets) using Franz diffusion cells.

Results: The optimised FLU-D NE was found to be 210 ± 5 nm in droplet size with PDI 0.14± 0.01, well-dispersed spherical droplets as shown in Figure 1. FLU-D NE was stable for 2 weeks at room temperature and at 8° C in terms of droplet size and PDI. The EE% was 99.81 ±0.1% with LC %of 14.5 ±0.01%. FLU-D NE loaded DMNs showed a sufficient mechanical and insertion properties to bypass the *stratum corneum* (SC). The novel FLU-D NE loaded DMNs formulation has an *in-vitro* skin dissolution < 10 m. This combined system of MNs and NE was able to deliver FLU-D transdermally.

Conclusions: Based on *in –vitro* studies, FLU-D NE MNs was able to bypass the stratum corneum of the skin and deliver FLU-D transdermally as illustrated in figure 8. These findings suggest that this oily lipophilic prodrug can be delivered transdermally using this novel combination of MNs and NE. For future work, the pharmacokinetics evaluation of FLU-D NE loaded DMNs will be performed in an animal model.