TRANSDERMAL LONG ACTING DELIVERY OF FLUPHENAZINE DECANOATE USING NOVEL POLYMERIC DISSOLVING MICRONEEDLE SYSTEMS.

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Background: Schizophrenia is a severe form of mental illness affecting about 7 per 1000 adults globally. Schizophrenia can be defined as a disturbance that must last for six months or longer, including one month of delusions, hallucinations, disorganized speech, grossly disorganized or negative symptoms. This mental disorder can be managed using medication, psychological and supportive treatment. Despite the critical importance of medication, nonadherence has been recognized as a problem worldwide and maybe the most challenging aspect of treating patients with schizophrenia. Cognitive impairment, lack of illness insight and symptom severity are part of the unique factors of nonadherence in schizophrenia. Nonadherence to medication results in relapse, rehospitalization, longer time to remission, and attempted suicide. Enhancing adherence to antipsychotic medications has the potential to reduce psychiatric morbidity and costs of care substantially. Fluphenazine Decanoate FLU-D is one of the long-acting antipsychotics used as a maintenance treatment of schizophrenia, it is administered as an intramuscular injection every 14-35 days. This long-acting injectable delivery system has overcome plasma drug fluctuations associated with the oral daily intake of the drug. However, FLU-D requires a professional health care provider and specific administration procedures. In addition to the pain and inconvenience of the typical hypodermic needle. Transdermal long-acting delivery of FLU-D using dissolving microneedle MN system has the potential to provide convenient noninvasive long-acting delivery of this lipophilic antipsychotic.

Methods: This research project started with developing a method of preparing dissolving MNs loaded with FLU-D. Firstly, an aqueous blend of 20%Polyvinylpyrrolidone PVP 29-32 KDA, 20% Polyvinyl Alcohol 10KDA and 10% w/w FLU-D was mixed for 15m at 3000 rpm by speed mixer. Secondly, almost 500 mg of this formulation was cast into LTS MNs moulds (600 MN, 750 μm). Followed by applying 5 bar pressure for 15m using the pressure chamber. The excess formulation was removed and MNs were lifted to dry for 24h at room temperature. To form the free-drug baseplate, 500 mg 50% PVP 360 KDA was added, followed by centrifugation for 15m at 3500rpm and dried for 24h at room temperature. To evaluate the physical ability of the formulated FLU-D loaded dissolving MNs, a compression force test was performed by attaching the MNs to a cylindrical probe of a TA.XT2 Texture analyser moving toward the steel baseplate and was held for 30 seconds at the force of 32 N per patch. The height of individual MNs was measured using Leica EZ4W stereo microscope before and after the test to determine the reduction of MNs height. Besides, to evaluate the insertion ability, MNs were inserted into full-thickness porcine skin manually and Optical coherence tomography OCT images were taken. Further, drug content in MNs was using a validated HPLC method.

Results: FLU-D loaded dissolving MNs showed good physical and insertion properties, the mean of %height reduction is 5.23 ± 0.91 and OCT images showed that the mean of inserted length is 528.05 ± 20.48 μm. In terms of drug content in MNs 0.99 ±, 0.18 mg per array was found.

Conclusions: A promising FlU-D loaded dissolving microneedles system has been developed. The viable physical and insertion properties of this system have been proved in addition to the drug content. Further in-vitro studies are required to address the drug release.