Rapidly Dissolving Microneedle Patches for Transdermal Iron Replenishment Therapy
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Purpose
Conventional therapy for treating iron deficiency suffers from incomplete absorption and invasive routes of administration and despite continuous efforts, iron deficiency anemia remains the most prevalent nutritional disorder. In this direction, the present study investigates the feasibility of using low molecular weight sodium hyaluronate (HA) dissolving microneedles as a transdermal therapy to treat iron deficiency anemia

Methods
Microneedles were fabricated by mold casting method. Master structure consisting of 10 x 10 arrays of pyramidal needles were degassed and PDMS (10:1 w/w ratio of prepolymer to curing agent) was then poured over the master structure and cured at 90°C for 1 hour. The cured PDMS was carefully peeled off to give inverse replicated PDMS molds. Sodium Hyaluronate (HA) (Bloomage Fred Biopharm USA INC. Parsippany, NJ) having a molecular weight of 10 kDa was used as the casting material. Briefly, 50% w/w solution of HA loaded with 250 mg/mL FPP was poured over the micromolds and centrifuged at 4150 X g for 5 minutes to depress the solution into mold cavities. Excess solution outside the cavities was pipetted out and replaced with blank solution of high molecular weight HA (30-40 kDa). The micromold was kept overnight in a desiccator to facilitate drying after which FPP loaded microneedles was detached from the molds. The fabricated microneedles (10x10 array) had a height of 500 μm with a 500 μm pitch. In vitro permeation studies were carried out by applying the microneedles patch on excised rat skin sandwiched between a donor and receiver in a Franz diffusion cell setup. The receiver compartment was filled with buffered saline adjusted to pH 5. 30 minutes after the application, the skin was washed, dissolved and analyzed for FPP. In vivo experiments were carried out in iron deficient anemic rats. Rats were divided into 3 groups (n=4). Placebo group, FPP-Passive group and microneedle group. FPP microneedles patches was applied to rats for 1 hour to ensure complete erosion of the needles in the skin. Iron was administered to the respective groups for 2 weeks. Blood samples were collected from all animals at different time points and analyzed for hematologic parameter (hemoglobin, RBC etc.,) using HM2 hematology system.

Results
The amount of FPP loaded in each microneedle patch was 92.5 μg. The amount of FPP delivery across the rat skin as determined from the in vitro permeation experiments was found to be 85.7 ± 7 μg. Application of FPP loaded microneedles patch in anemic rats resulted in rapid and significant improvement in the Hematological parameters such as serum iron, Hemoglobin and RBC counts, within three weeks of treatment.

Conclusion
The study successfully demonstrated the feasibility of transdermal therapy to treat iron deficiency anemia using rapidly dissolving microneedles patches loaded with FPP.