

OBJECTIVE

The objective of the research was to assess the feasibility of delivery of Iron-Dextran via transdermal route with the aid of microneedles to treat Iron Deficiency Anemia in hairless rat model.

INTRODUCTION

➤ Anemia is a condition in which decrease in number of red blood cells (RBC's) or less than normal quantity of hemoglobin in blood. Globally, anemia affects 1.62 billion people which corresponds to 24.8% of population (2005).

➤ Iron deficiency anemia (IDA) is treated using iron supplements. Oral iron therapy is of limited potential in conditions where patients suffer with severe anemia due to heavy blood loss, gastrectomy; hence parenteral therapy is inevitable. Iron-Dextran complex is the only FDA approved iron source for parenteral administration. Parenteral administration of Iron-Dextran is associated with systemic side effects and anaphylactic reactions. Moreover, as parenteral administration is invasive, frequent administration is not acceptable. Therefore, there is need to develop a noninvasive method of delivering Iron-Dextran to treat IDA in a patient compliant way.

➤ As Iron-Dextran is a large colloid (Mol Wt 150 kDa - 250 kDa), passive delivery is not possible. Therefore microneedle mediated delivery is best suited.

METHODS

➤ *In vitro* studies were carried out using Franz diffusion apparatus.

➤ Freshly excised hairless rat skin was obtained and was placed between donor compartment which was filled with 200 μ L of 50mg/mL Iron-Dextran solution and receiver compartment with 5mL of phosphate buffered saline (pH 7.4) after pretreating the skin with custom made microneedles (650 μ m height) made of stainless steel.

➤ Untreated skin was used as control.

➤ Samples collected at different time points (0,2,3,4,5 and 6 h) and iron content was measured with FerroVer® reagent method at 510nm using UV-Visible spectrophotometer.

➤ *In vivo* studies were carried out in anemia induced hairless rats.

➤ Transdermal patch (20 cm²) loaded with 150 μ L of Iron-Dextran (50 mg/mL) was placed on the dorsal side of the rat pretreated with microneedles for a duration of 6 h every alternate day for 3 weeks.

➤ Blood samples were drawn and subjected to hematological studies using VetScan HM2 hematology system (Abaxis Inc., Union city, CA) at the beginning of study to find the basal values and at the end of 2nd and 3rd week.

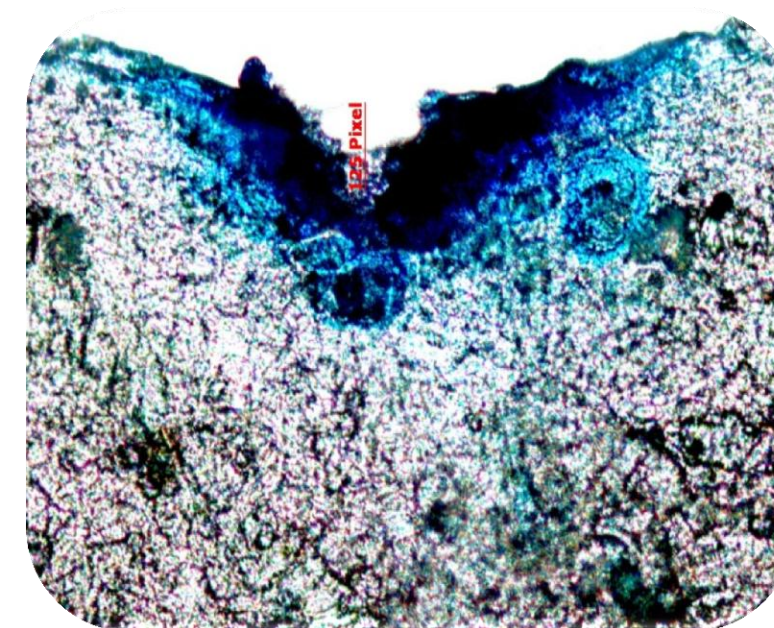


Fig 1: Representative picture showing the pore created by microneedle on the hairless rat skin (10 X)

RESULTS

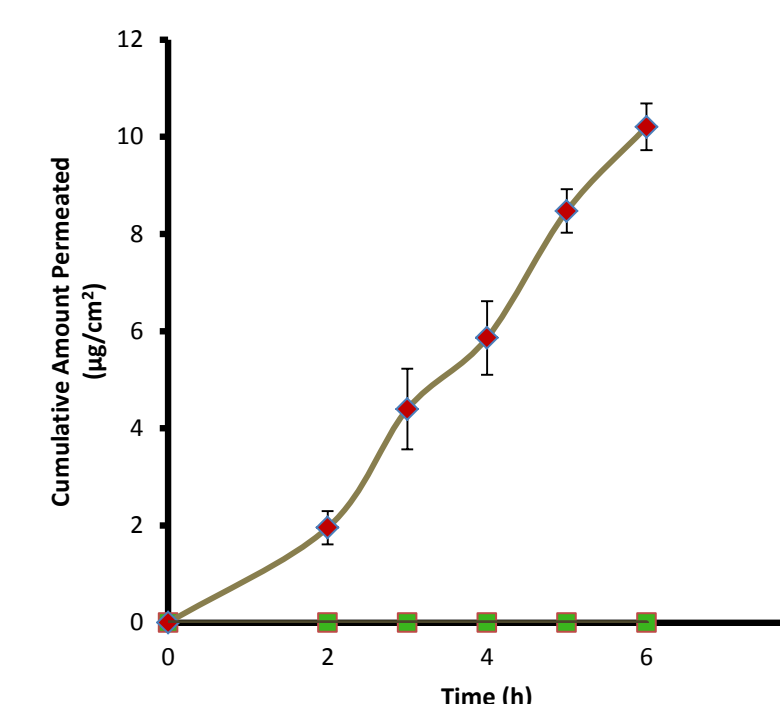


Fig 2: *In vitro* permeation of Iron-Dextran across hairless rat skin

➤ Results from *in vitro* studies concluded that, in case of passive mode of delivery there was no Iron-Dextran in the skin or in the receiver compartment.

➤ Whereas, in case of microneedle mediated delivery, the amount of Iron-Dextran permeated into receiver compartment at the end of 6 h was 10.20 \pm 0.48 μ g/cm² and the skin content (estimated by homogenizing the diffusion area in 1M sodium hydroxide) was 24.6 \pm 1.8 μ g/cm².

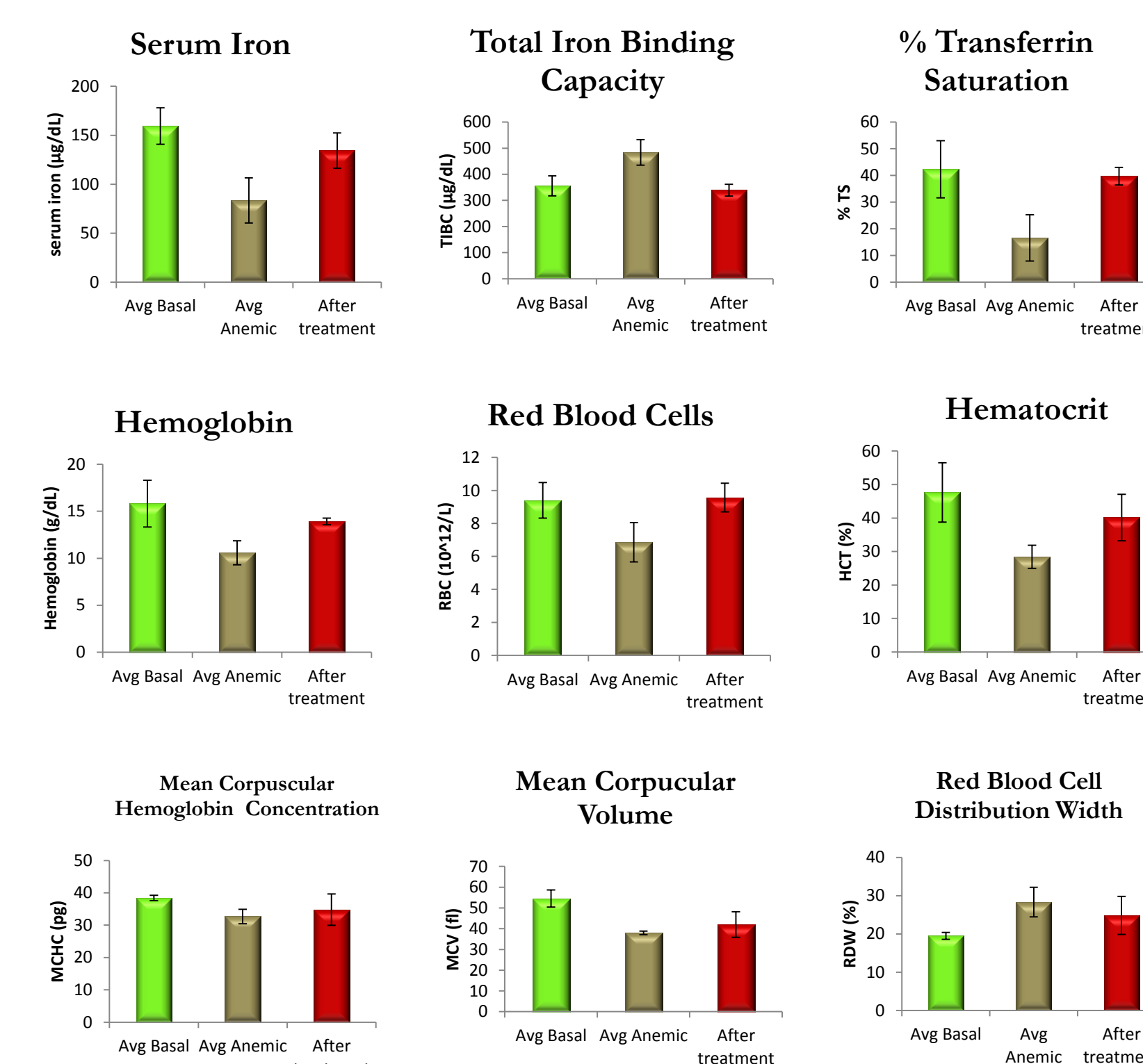


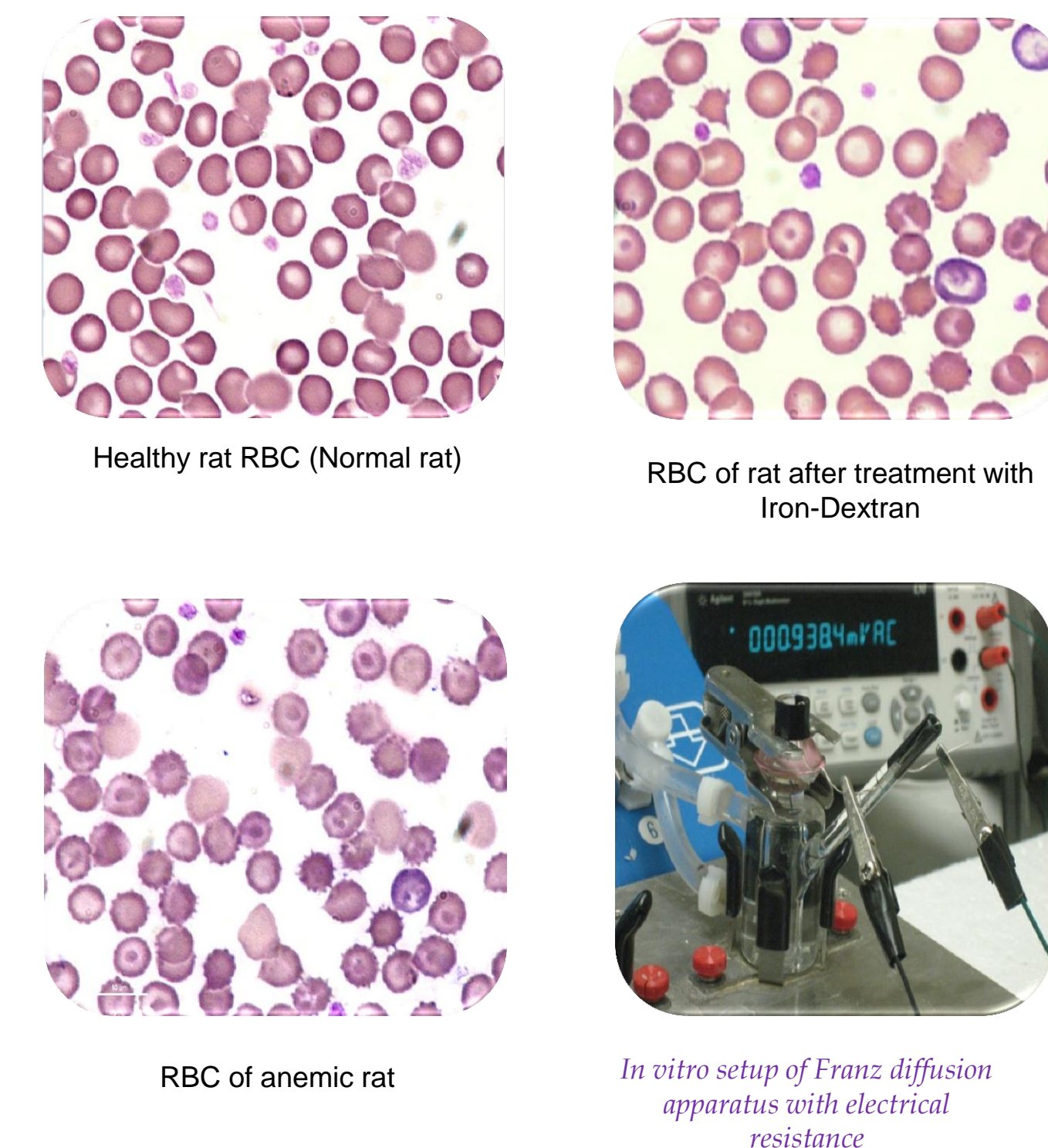
Fig 3: Hematological studies carried out in anemic rats to test the efficacy of transdermal administration of Iron-Dextran

➤ Biochemical parameters such as serum iron, total iron binding capacity and % transferrin saturation was estimated using *in vitro* diagnostic kits.

➤ The hemoglobin content in the anemic rats was increased from 10.58 \pm 1.23 to 13.65 \pm 0.63 and 13.92 \pm 0.32 g/dL at the end of 2nd and 3rd week respectively.

ACKNOWLEDGEMENT

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CONCLUSION

➤ Therapeutic levels of Iron-Dextran could be delivered transdermally using microneedle pretreatment (Poke and Patch method). The transdermal delivery has successfully restored the iron levels in the anemic rat model and serves as a potential alternative to parenteral administration of Iron-Dextran.