

The different groups were received as follows, group 1 (diabetic rats) was received oral insulin formula (F.C. = 7 IU/ml) using gavage needle. Group 2 (diabetic) was injected subcutaneously Rh-insulin solution (F.C. = 1 IU/ml). Group 3 (diabetic) was received intragastrically oral placebo preparation (nanoparticles dispersion without insulin) and used as control. Group 4 (normal rats) was received oral insulin formula (F.C. = 7 IU/ml). Group 5 (normal) was injected subcutaneously with Rh-insulin solution (F.C. = 1 IU/ml).

Blood samples were collected from the tail veins of rats prior to drug administration and at different time intervals (0, 1, 2, 3, 4, 6, 8, 10 and 18 h) and blood glucose level time profiles were constructed after dose administration using blood glucose level at zero time interval as a base line to glucose level in the later blood samples. The blood glucose was then determined by a glucose meter.

### **2.3.5. Measurement the intestinal absorption of insulin-loaded nanoparticles by everted gut sac model**

Rats were sacrificed by chloroform overdose sprinkled to a piece of cotton wool in a glass container equipped with a lid. The abdomen was opened by a midline incision; the whole of the small intestine was then removed by cutting across the upper end of the duodenum and the lower end of the ileum. The small intestine was then washed with normal saline solution (0.9% w/v NaCl) using a syringe equipped with blunt end.

The isolated small intestine was cut into 2 pieces each about 15 cm; approximate diameter of intestine was 0.8 cm. To evert the gut, a stainless steel rod (300 mm long, 1-5 mm diameter) was used to push the ileal end of the gut, into the gut lumen until it