Hepcidin as iron chelation target in Beta Thalassemia Major: An *in-silico* approach

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ABSTRACT

Beta-thalassemia major medical treatment primarily requires the transfusion of blood which majorly founds in infant population. Approximately 200 mg of elemental iron is present in each red blood cell (RBCs)transfusion unit. Hepcidin is a small hepatocyte-secreted peptide hormone that circulates in blood plasma and is excreted in urine. Hepcidin regulates the concentration of iron in plasma and the distribution of iron between tissues. Many iron disorders underline deregulation of the production of hepcidin. Chronic hepcidin surplus induces iron-restricted anaemia, while hepcidin deficiency results in iron excess and other parenchyma with iron deposition in the liver. Elevated hepcidin level causes inflammatory conditions which activates the transporter ferroportin (FPN) for excess iron removal. Hepcidin is regulated by plasma iron transferrin and intracellular iron stores, these signals likely utilize the bone morphogenetic protein (BMP) pathway to alter hepcidin expression. As an effective technique to combat the iron excess in beta thalassemia major, inhibiting hepcidin-mediated ferroportin (FPN) degradation is proposed in this study. A systematic *In-silico* approach initiates with detection of hepcidin binding inhibitors to increase the excess iron removal. Multiple signalling pathways such as the BMP-SMAD pathway and IL-6 via JAK STAT3 pathway control hepcidin output from hepatocytes. The prevailing approach focused to avoid hepcidin-mediated FPN degradation, including inhibition of hepcidin expression through the use of anti-hepcidin compounds and FPN binding agents. Virtual screening of natural compounds and synthetic chemical compounds by molecular docking approach will be used to find the promising inhibitor against hepcidin.

Keywords: Hepcidin inhibition; Beta thalassemia major; Virtual Screening

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