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## **Beneficial and anti-fibrotic effect of surface engineered nano-formulation of crocetin on experimental induced peritoneal fibrosis: novel approaches for peritoneal dialysis**

**Deeksha Chauhan**<sup>1</sup>, Vikas Kumar<sup>2</sup>

<sup>1</sup>Department of Applied Physics, Allahabad University, India

<sup>2</sup>Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology & Sciences, India

**Objectives:** Peritoneal dialysis (PD) is widely accepted alternative to hemodialysis in the treatment of end stage renal disease. Recent studies suggest that PD is effective for initial two year on patient with renal replacement therapy and long term treatment can cause inflammation, fibrosis of peritoneal membrane (PM), neoangiogenesis etc. Activation of TGF- $\beta$ /Smad pathway can lead to inflammation, neoangiogenesis important in alteration of PM with PD. Now, targeting the TGF- $\beta$  signaling pathway is consider as the novel approach to treat PD complications. Here, we investigated the beneficial effect of Crocetin (CT) in Wistar rat having peritoneal fibrosis (PF).

**Methods:** Emulsion solvent technique was used for the preparation of CT loaded PLGA nanoparticles (CT-PLGA-NP). The CT-PLGA-NP was developed via cost-effective doses system and tested for their potential to reduce transforming growth factor- $\beta$  (TGF- $\beta$ ) signalling via docking. Intraperitoneal injection of Chlorhexidine gluconate (0.1%) was used to induce the PF in rats. Inflammatory and biochemical parameters were scrutinized, respectively. Immunofluorescence and immunohistochemistry techniques were used for the estimation of fibrosis associated factor.

**Results:** CT-PLGA-NP exhibited the a desired nano particles which are spherical and smooth in nature and relatively small size distribution. Docking analysis suggest that CT was snugly fitted into the inner groove of allosteric site of TGF- $\beta$  via making selectively and efficiently interaction with ALA41, ILE22, VAL106 and VAL107 protein receptor protein with Ki ranging from 554 nm to 4.34  $\mu$ M disclosing as potential effect. CT exhibited the considerably down-regulation of peritoneal membrane thickness and expression of myofibroblasts with avoidance of loss filtration of peritoneal membrane. CT significantly reduced the neoangiogenesis and proinflammatory chemicals like TNF Alpha (72%), MCP -1 (52%) and IL- 1 Beta (48%) when compared to standard PG group.

**Conclusions:** Crocetin down-regulated the experimental peritoneal fibrosis via alteration of TGF- $\beta$ /Smad pathway and suggested the potential strategy for treating long term Peritoneal dialysis complications.