Comments and Suggestions for Authors are in *italics*

*This reviewer has the following minor suggestions to be considered by the authors:*

-Please, specify why, out of numerous contributors/cell signalling pathways in pathogenesis of hepatic fibrosis, the endocannabinoid and apelin systems were chosen.

Since there are no effective curative therapies yet to treat liver fibrosis we chose endocannabinoid and apelin systems as novel promising signalling pathways, as reflected in the literature, to reduce hepatic stellate cell activation and liver fibrosis.

-While both endocannabinoid and apelin systems are comprehensively described, less attention was devoted to general mechanisms of hepatic fibrosis. This reviewer believes that this manuscript will significantly benefit by adding a section on pathogenesis of hepatic fibrosis as well fibrosis-preceding pathological states, such as (non)-alcoholic fatty liver disease.

As suggested by the reviewer we added a paragraph in the introduction about the pathogenesis of hepatic fibrosis and NAFLD in the new version of the manuscript (lines 33 – 39, and new references number 2 and 3). We consider this new section part of the introduction as the rest of the review focuses on the precise mechanisms of the endocannabinoid and apelin systems on liver fibrosis.

-Lines 191-193 - please, elaborate more on the data available from the CCl4-treated rats and effects associated with administration of selective CB1 antagonists: are these effects considered positive or negative?

As suggested by the reviewer we have expanded the data available from the CCl4-treated rats and effects associated with administration of selective CB1 antagonists in the new version of the manuscript (lines 245 - 249, and new reference number 99). These effects are considered positive as CB1 antagonists increase the arterial pressure in cirrhotic rats but not in healthy animals, and they also reduce the expression of pro-fibrogenic and pro-inflammatory factors in cirrhotic animals.