Peer Review File

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Reviewer A

The investigators have looked into the neuroprotective role of PQQ after SCI in rats. Their results suggest that PQQ down-regulates the expressions of IL-1β, TNF-α and IL-6, inhibited apoptosis after SCI, and inhibit LPS-induced apoptosis and inflammation of astrocytes. This is a well written manuscript, and the results are well presented. Would recommend publication.

Reviewer B

In the current manuscript #67947, the authors have evaluated the role of Pyrroloquinoline quinone (PQQ) evaluated the role in inflammation, apoptosis, and autophagy after Spinal cord injury (SCI) in rats. The study results suggest that PQQ could enhance functional recovery, increase the neuronal number, and have an anti-inflammatory effect. Authors did experiments to support the previously reported findings of PQQ (PMID: 19026989, 25820784, PMC3303106, and many more). Overall manuscript is linear. However, certain points need to be addressed before considering this manuscript.

Comment 1: The title "Effect and mechanism of Pyrroloquinoline quinine on SCI in rat" is broad; I would suggest editing as per the findings. The authors broadly focused on inflammation and apoptosis.

Reply: According the comment, the title will be revised as "Inhibit inflammation and apoptosis of pyrroloquinoline on SCI in rat".

Changes in the text: We have modified our text as advised (see Page 1, line 3).

Comment 2: Please clearly mention the dosing schedule, the time point of animal sacrifice, and biochemical parameters shown in the figures.

Reply: According to the comment, we described the dosing, and the time point of animal sacrifice, and biochemical parameters shown in the figures.

Changes in the text: We have modified our text as advised (see Page 38, line 2-6, line 9-11).

Comment 3: The authors mentioned that the BBB score is related to histopathological changes after SCI. The statement is not correct. Please correct.

Reply: According to the comment, we described the BBB score and histopathological in different paragraph respectively, for avoiding that there is relationship between the

BBB score and histopathological changes when they are in the same paragraph.
Changes in the text: We have modified our text as advised (see Page 14, line 11-22; Page 15, line 1-19).

Comment 4: Post-operative care is more manageable in females then why do the authors choose male rats in the experiments?
Reply: Because the estrogen level of female rats is not well regulated, the level of estrogen will affect some experimental results such as inflammatory response, so we choose male rats to do SCI model.
Changes in the text: There is no any change in the text.

Comment 5: Figure 1 HE and Nissl staining background does not seem to be uniform across all groups. The authors should represent a uniform area in zoom images; the central canal is at different levels in image E-H. Moreover, the authors should highlight the injured area in SCI+PQQ. The image I-L are not giving any extra information. Please mention the time point for IL-1β, IL-6, and TNF-α expression.
Reply: According to the comment, we have modified the picture and added the corresponding information.
Changes in the text: We have modified our text as advised (see Figure1; Page 37, line 21-22; Page 38, line 1-14).

Comment 6: Authors reported an increase in AKT expression in SCI; however, it contrasts with previously published reports that suggest that AKT expression downregulates after SCI.
Reply: It is indeed reported that the expression of AKT was downregulates after SCI, but there are also reports (PMID: 28981091 PMCID: PMC5682656) that the expression of AKT is increased after SCI, which is consistent with the results of this study.
Changes in the text: There is no any change in the text.