Dr Çimen Karasu,

Editor,

You can find the answers and explanations of the corrections below for the comments of Reviewer A.

a)Major

*1. It is known that EDCS are augmented by aging, hypertension, high glucose and diabetes. Hence the aim and the originality of the findings of this study must clearly defined. The whole text needs extensive revision, including abstract.*

*For example:*

*Abstract: aim, methods and conclusion must be rewritten clearly (There is no aim and method in the abstract).* **The abstract reviewed as requested and sections were organized and rewritten according to the reviewer’s comments.**

*Please insert Turkish abstract and key words in the manuscript.* **The Turkish abstract and key words were added.**

*Introduction: needs to be rewritten to clearly demonstrate the study importance, objectives of the study have to be clearly delineated.* **The aim and rationale of the study explained as requested.**

*Please give appropriate references in introduction section (for ex 1,2,5-check!!).* **The reference list was checked and the wrong citations were corrected.**

*Please give the contractile mechanism of A23187 in introduction section. (for what purpose did you use this agent as a tool in your experiments etc.).* **The action mechanism of the A23187 was elucidated properly in introduction section.**

*Method: There are some confusing information, for ex. “endothelium denuded preparations”: did you use them?* **In the present study, only endothelium-intact preparations were used. This statement in Methods section was removed.**

*Please mention that you used isolated organ chamber/bath, etc.* **The statement for organ bath usage was corrected as “...The rings were mounted between two hooks attached to an isometric force transducer connected to a data acquisition system (Biopac, MP30, CA, USA) for continuous recording of tension. The preparations were suspended in 10-ml tissue baths containing oxygenated Krebs solution at 37°C...”.**

*You should give dissolving information for A23187.* **The solubility properties of the A23187 was inserted in Methods section under the heading of “Reagents”.**

*Results: please dont mention methodology again here,* **The statements were removed as requested.**

*and check the sentences.; what means “ control level “* **As explained in Results section, the statement “control level” indicates the A23187-mediated contractile response at the concentration of 10uM of the isolated thoracic aorta preparations of 34-week-old rats in normoglycemic conditions without any incubation. You can find the explanation in Results section as following “…For following experiments, A23187-mediated contractile responses were obtained from aortic rings prepared from 34-week-old rats and the Emax value of A23187-mediated contractile response of 34-week-old rats (14,41±0,81%) was referred as control indicating normoglycemic conditions without any incubation period.”**

*did you use high glucose medium in aortae from 34- w animals? Please specify.* **The hyperglycemic conditions were applied only isolated aortic preparations of 34-week-old rats.**

*Figs, y axis: please specify “tension” or “tension change” as % of KCl.* **In Figures, the labels of the y-axis were corrected as “Tension (%KCl: 60mM)”.**

*In figure 2 -legend: 34-w old rats? Please specify /insert; n:2-5? Which gruop n: 2? Is this sufficent for analysis?* **As explained in Results section, only 34-week-old rats were used in the experiments graphed as Figure 2. The normoglycemia plus mannitol (11mM glucose+14mM mannitol; NG+MN) group had only two separate and independent results (n=2). It is clear that “n=2” is not sufficient for statistical analysis. However, normoglycemia plus mannitol group was not included in a statistical analysis in the given graph, this group was organized only to check the effect of osmotic pressure induced by high concentration of glucose on A23187-mediated contractile responses. The requested explanations for both of the comments were inserted in the Legend of the Figure 2.**

*Discussion: Must be revised giving importance of the results, and must be paralelled with the aim. Discuss with similar /contradictory findings; and needs recent findings/references etc.*

*What are the possible mechanisms about disapperance of A23187-induced contractions by the time? Can you give supportive information/references?* **The possible mechanism was discussed in Discussion section with references.**

*Limitation of the study is very important point. ED-vasodilations shoul be tested and compared; or at least Phe-vasoconstrictor responses should be tested and compared.*

*b) Stylistic*

*Abstract: It’s better not to use abbrevations for EDRF, EDHF and EDCF at first mention.* **The abbreviations were removed from Abstract section.**

*References: according to the journal regulations please abbrevate the journal names.* **The requested corrections were done.**

*Text: Please check the text for language mistakes.* **An extensive stylistic check was performed carefully.**