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REVIEWER'S REPORT

Manuscript No.: IJAR-55951

Title: ACTIVATION OF NRF2/HO-1 SIGNALING MEDIATES THE PROTECTIVE EFFECTS OF HIBISCUS SABDARIFFA AGAINST RESTRAINT STRESS–INDUCED OXIDATIVE DAMAGE IN FEMALE WISTAR RATS

Recommendation:
Accept as it is .....
Accept after minor revision...
.....
Accept after major revision .....

Rating	Excel.	Good	Fair	Poor
Originality		Good		
Techn. Quality	Excellent			
Clarity	Excellent			
Significance	Excellent			

Reviewer Name: Dr.Sumathi

Detailed Reviewer's Report

1. **Rosella (Hibiscus sabdariffa) is also known as 'hibiscus flower' which can sometimes lead to confusion as there are over 260 species in the hibiscus genus, and there are two other species also well-known for their edible flowers—the iconic tropical hibiscus (H. syriacus) and Chinese hibiscus (H. rosa-sinensis).**
2. **Toxicity: Hibiscus sabdariffa is not toxic to humans or animals. In fact, it is often consumed as a food and beverage ingredient. However, as with any plant, it is important to consume it in moderation and ensure it is prepared properly.**
3. **The Nrf2/HO-1 pathway is a critical cellular defense mechanism that protects against oxidative stress, inflammation, and damage. Nrf2 (nuclear factor erythroid 2-related factor) acts as a master transcription factor that, when activated, induces the expression of antioxidant genes, most notably HO-1 (heme oxygenase-1), to promote detoxification, cell survival, and homeostasis.**
4. **Oxidative stress is an imbalance between the production of harmful, unstable molecules called free radicals (or reactive oxygen species, ROS) and the body's antioxidant defenses, leading to potential cell**

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and tissue damage. It is caused by factors like diet, lifestyle, and environmental stressors, playing a key role in aging and chronic diseases.

5. **Restraint stress (RS) is a widely used lab model where animals (like rats/mice) are physically immobilized to induce psychological/physiological stress, triggering anxiety, depression-like behaviors, and changes in hormones (corticosterone), brain activity, and the immune system, helping researchers study stress-related disorders and treatments. It involves confining animals for varying periods, leading to measurable effects on cognition, emotion, and bodily functions, with acute vs. chronic exposure causing different long-term impacts.**
6. **Inflammation is the body's natural immune response to harmful stimuli—such as pathogens, injuries, or toxins—designed to protect tissues and initiate healing. It involves increased blood flow, white blood cell activity, and fluid leakage, often causing hallmark symptoms like redness, heat, swelling, pain, and loss of function.**
7. **Antioxidant enzymes are proteins that protect cells from damage by neutralizing harmful molecules called reactive oxygen species (ROS) and reactive nitrogen species (RNS), acting as the body's primary defense against oxidative stress. Key examples include Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione Peroxidase (GPx), which convert dangerous free radicals into harmless substances like water and oxygen, maintaining cellular health.**
8. **Key words are excellent to understand.**
9. **Abstract and methodology part are awesome with meaningful.**
10. **Result part is excellent with picture, tables and graphs.**
11. **Significant points are given appreciable!.**
12. **Summary points should be added.**
13. **References should be in alphabetical order.**
14. **After a small changes good to publish in your journal.**