Reviewer 1 (Souvik Karmakar)

Basic reporting

This study is very innovative, and hypothesis directed. I feel they did most of the experiments to prove their hypothesis. I feel the following may be necessary to be included in the paper,

1. UV could change the property of fibroblast, but how it is correlating with aging skin fibroblasts.

Answer : You can see the mechanism of UV affecting skin fibroblast in row 42-46 and 58-63.

2. Was the supernatant collected on the last day or everyday during CA treatment?

Answer : The supernatant collected on the last day of CA treatment.

Experimental design

I think IL-1β and TNFα results should be in one figure instead of two.

Answer : The data about IL-1β and TNF-α merged already

Fig 3. and Fig. 5 should be in the supplementary section.

After removing the CA treatment, how long did the fibroblast show less production of IL-1β, TNFα and ROS?

Answer : We didn't measure the production of IL-1β, TNF-α, and ROS after removal of CA. We only measured the IL-1β, TNF-α, and ROS after CA treatment.

Validity of the findings

I think this study is unique and all the points they covered in this study are crucial to show the effect of CA in a aging skin.

Comments for the Author

This study is well designed and shows the effect of natural product on anti-inflammatory responses in skin. I have suggested few concerns. The paper seems to shed light in the area of skin immunology.

Reviewer 2 (Anonymous)

Basic reporting

Chlorogenic Acid is an interesting compound to study. It appears a lot of work has already been done on it. The perspective of using UV as an insult is interesting. However multiple concerns need to be addressed. The authors must address the language in the paper and make grammatical corrections all throughout the paper.

Experimental design

Only 1 cell line has been tested which is inadequate

Answer : We're sorry, but in this research we only used 1 cell line to describe the effect Chlorogenic Acid (CA) to UV induced-skin fibroblast cells which is BJ cell line.

Validity of the findings

This study is done in 1 cell line therefore replication of findings in at least 2 more cell lines is required to increase the impact of the outcome and validity of this study.

Comments for the Author

Overall, it is an interesting area. However, multiple issues need to be addressed to ensure better quality of the paper. My concerns are as follows

In introduction - Mention other external factors that affect skin aging. Add more background to the pathways being addressed

Answer : External factors already added and the pathway about UV-induced skin aging already added.

Line 36 – Why especially in women? Does skin aging happen only/more in women? Or is there is a reason why it is more of a problem in women than men?

Answer : Because the skin aging problem is more problem in women because the beauty reason. The skin aging happen in men and women.

Lines 50-51, add references for this statement- The inhibition of oxidative stress now becomes an important approach for treating skin damage due to aging.

Answer : The references already added.

Materials – Lines 65-69 – Why are cells treated with multiple antibacterial and antimycotic agents? What were the controls and were they in a separate incubator?

Answer : Cells treated with multiple antibacterial and antimycotic agents to prevent the contamination in the laboratory. The control used in this research is (1) normal control (untreated cells) (2) BJ cells + DMSO 1% (vehicle control whether DMSO toxic or not to cell, DMSO for solving CA, DMSO is safe solvent but we must check toward skin fibroblast cells) (3) UV-induced BJ cells (positive control). They weren't in separate incubator.

How was the 75-minute UV exposure decided? What kind of UV?

Answer : The 75 minutes UV exposure is based on optimization at our laboratory, more 75 minute all cells are death, we evaluate on aging skin cells, apart of them were damaged, high ROS level (based on flowcytometry data). The UV used in this research is UVC type

It is important to make sure the study is repeated in at least 2 more cell lines for the study to be acceptable.

Answer : As we already mentioned, this research focused on the effect of CA on UV-induced skin aging cell line that is BJ cell line only.

Line 80 – What is meant by a normal control? Also, 1% DMSO is quite high, DMSO should be in 1:1000 ratio, any reason for 1% DMSO? Also, there should be another control group of DMSO with UV.

Answer : BJ cells without treatment (or negative control or control group, skin fibroblast cells were uninduced by UV). From the most of journal the solvent used usually DMSO 1% so we used that concentration, this concentration safe for cells and can dilute well the substance (Chlorogenic acid)

Line 85- What is mg protein?

Answer : The mg protein define the protein content in each sample used in ELISA based on Bradford assay used to measure total protein for each sample (normal control, positive control, CA).

Bar graphs are presented in a complicated manner and the significance is difficult to understand. Also, why are 2 methods of representation needed –pg/ml and pg/mgprotein?

Answer : The data presentation used pg/ml and pg/mg protein because this to know the ratio of antigen detected with mL sample and mg protein from each sample

Line 148 and 161- State what the significant difference to controls are.

Answer : The treatment data compared with positive control (UV-induced BJ cells) and the significant difference measured by statistic.

Note: DMSO affects number of apoptotic cells, reinstating the importance of reducing amount of DMSO and using that as a control. DMSO 1% was same with negative control (untreated cells).

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