Title: ACACIA HONEY ACCELERATES IN VITRO CORNEAL ULCER WOUND HEALING MODEL

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Version: 1 Date: 01 Jul 2016

Author’s response to reviews:

RESPONSE TO REVIEWER’S COMMENTS

Reviewer #1: The paper is interesting.

Thanks for the compliments.

I have some question regarding this paper:

1) Was the Acacia Honey cytotoxic?. This is important to establish the safety of the product.

No, the Acacia honey was not cytotoxic. We have already done an earlier study (ref no. 9: Ker-Woon et.al. Effect of acacia honey on cultured rabbit corneal keratocytes. BMC Cell Biol 2014; 26:15:19 doi: 10.1186/1471-2121-15-19) which showed that AH at the range of 0%-3.125% was not cytotoxic to corneal keratocytes using H2O2 at the concentration of 1.56nM as positive control. This fact has been included in the Materials & Methods section (pp 5, line no: 10-13).
D) The manuscript would benefit from inclusion of introducing/bridging sentences between the individual parts of the "Results" that explain the logical order and rationale for the experiments.

We have incorporated the facts in the results section. The rationale of each parameter studied was explained at the very beginning of each section of the results (pp: 9, line 12; pp: 10, line 2; pp: 11, line 6).

Reviewer #2: i) Only one concentration was used. This deserves discussions about the rigid choice.

We had conducted and published a study (Ker-Woon et.al. Effect of acacia honey on cultured rabbit corneal keratocytes. BMC Cell Biol 2014; 26:15:19 doi: 10.1186/1471-2121-15-19) using AH at the concentration of 0% - 3.125% to select the optimal concentration for proliferation of corneal keratocytes (ref no: 9). These facts were already discussed in the text under the Materials and methods section. Hence, we believe that we have addressed the issue regarding only one concentration used.

ii) No positive control e.g. steroidal preparation, was used, please discuss.

This is to explain that steroidal preparation is not advocated for conventional treatment in corneal wound healing. This is because steroids cause delay in wound healing. The usual practice among ophthalmologist is to prescribe antibiotic eye drops as prophylaxis to prevent secondary infection.

The present study involved creating a clean wound onto confluent monolayer corneal fibroblast culture. This is to mimic the corneal ulcer due to trauma and not due to any infective cause. Hence, the omission of the positive control with any drug for e.g. steroids or antibiotics is justified.

We have also added this fact at the end of the discussion (pp: 15, line 10 - 11).