Comparative *in vivo* evaluation of three types of honey on topical wound healing activity in rabbits

Nagiat T Hwisa, Prakash Katakam*†, Babu Rao Chandu, Einas Ghafar Abadi and Ebtihal Mosbah Shefha
Department of Pharmacology and Biochemistry, Faculty of Pharmacy, University of Zawia, Al-Zawia, Libya.

**ARTICLE INFO**

*Article history:*
Received on: 31/03/2013  
Revised on: 09/07/2013  
Accepted on: 08/08/2013  
Available online: 30/08/2013

**Key words:** Honey, Sidr, Thyme, Spring, wound healing, topical.

**ABSTRACT**

The present investigation has focused on the comparative evaluation of topical wound healing activity in rabbits using three types of honeys such as Sidr (SDH), Thyme (TYH), Spring (SPH). The activity was compared with commercial wound healing formulations, Mebo (MBC) and Fusidin (FSC) creams. Among the different types of honey SDH was found to possess higher healing rate of wounds induced either by thermal or chemical methods. Whereas, in thermal induced burns, both TYH and SPH have shown similar wound healing activity but better than that of standard drugs. The activity for thermal and chemical induced burns was found in the order of SDH > TYH/SPH > MBC > control and SDH > TYH > SPH > FSC > control respectively. Among the three tested honeys, the t-test data was compared to those of controls and it was found that there was a significant (p<0.05) reduction in the wound area. It was concluded that honey in general could be employed as a natural topical wound healing agent comparable to commercial synthetic analogs tested in the study. Further the present investigation proves that SDH is possessing superior wound healing activity than that of TYH and SPH.

**INTRODUCTION**

Honey is the sweet, viscous fluid produced by honey bees (the genus *Apis*) using the nectar of flowers. Historically, honey has been used by humans to treat a variety of ailments, from gastric disturbances to ulcers, wounds and burns, through ingestion (Visavadia et al., 2008). It maintains a moist wound environment within the wound environment from recent clinical studies (Visavadi et al., 2008). It prevents the growth of bacteria by releasing anti-inflammatory cytokines and growth factors (Henriques et al., 2006; Tonks et al., 2003). Its effectiveness in rapidly clearing up the infection and promoting healing is not surprising in light of the large number of research findings on its antibacterial activity. The precise composition of honey varies according to the plant origin on which the bee feeds. (Rakha et al., 2008; Al-Mamary et al., 2002). Sidr honey is most revered honey and expensive honey in the world. It is obtained from the flowers of the ancient Sidr tree (*Ziziphus spina-christi*). Sidr tree grows in coastal, desert, and semi-desert areas and found extensively in the eastern part of Yemen. (Sidr Honey^A,^ 2013).
Thyme honey also known as Greek thyme honey is light coloured and, infused with layers of flavour from the abundant wild flowers carpeting the mountains in spring and summer. The presence of phenol is known for its antibacterial activity (Greek Thyme Honey, 2013). Wide medicinal applications are associated with spring honey. It strengthens the memory and resists aging, diabetes and diarrhoea (Spring Honey, 2013).

From the literature survey we have found that there is no research carried out on comparative evaluation of wound healing activity of honey from different types and sources. Therefore the present investigation is focused on the comparative evaluation of topical wound healing activity using three types of honey.

MATERIALS AND METHODS

Fusidin cream (FSC) (sodium fusidate 2% w/w ointment, Leo Pharmaceutical Products, Denmark. Batch No. EG3794), Mebo cream (MBC) (0.25% w/w β-sitosterol, Gulf Pharmaceutical Industries, UAE. Batch No. 509), Sidr honey (SDH), Thyme honey (TYH), Spring honey (SPH) were procured from local market. Conc HCl was of analytical grade from Merck, Germany.

Experimental protocol

A prior permission from the institutional animal ethics committee was obtained by the researchers to conduct the present investigation on White New Zealand rabbits. The animals were housed under standard laboratory conditions, maintained under 12/12 h light/dark cycle and fed with commercial foods such as crushed wheat and corn along with distilled water ad libitum. Each group consisting of five rabbits weighing about 1.5 to 3.0 kg was selected randomly for the study. The healthy rabbits of either sex were divided into five groups consisting of five animals in each group. Group 1 received FSC or MBC as a standard group. Group 2 received SDH, group 3 received SPH and group 4 received TYH. Group 5 animals were maintained untreated as a control. The wound healing activity was tested as per the modified procedures of literature (Mekonnen et al., 2013; Abu-Zinadah, 2009).

Induction of wound

Primary irritation to the skin was measured by a patch-test technique on the intact skin of the rabbits in accordance with the guidelines of the Consumer Product Safety Commission, Title 16, Chapter II, Part 1500 (Bonnette et al., 2001; Derelanko and Hollinger, 2001, Yogeshwar and Vandana, 2010). Topical wound was induced in all groups by chemical and thermal means. The chemically induced wound was affected by spreading few drops of conc. HCl 35% v/v upon the shaved skin of rabbits as described by Arwa (2011) and Abu-Zinadah (2009) and is shown in Fig. 1B.

The wound healing activity in thermal induced burns was found to be in the order of SDH > TYH/SPH > MBC > control. The results showed that there is a considerable wound healing activity among the treated groups over control. The wound healing activity of the treated groups was measured in terms of decrease in the area of the wounds caused by the burns.

In the present investigation, thermal injury was chosen as an alternative to mechanical injury of the skin of rabbits (Borhan, 2012). In the thermally induced burns, after the treatment period of 4 weeks, the wound in group 1 (standard, MBC) animals were found to be 3.38 cm, whereas as in group 2 (SDH treated) the areas of wound were reduced to 2.36 cm. In group 3 (SPH treated) and group 4 (TYH treated) the area of wound was found to be same with 2.92 mm². The group 5 (untreated control) showed a decrease in the wound area with 3.41 mm² owing to the natural phenomenon of healing process. The results are shown in Table 1 and Fig. 3. The wound healing activity in thermal induced burns was found to be in the order of SDH > TYH/SPH > MBC > control. The results indicated that the three types of honey used in the study were found to be having a significant wound healing
activity than that of standard used. Among the different types of the honey SDH was found to possess higher wound healing rate as against thermally induced wound. In chemical induced wounds, after the treatment period of four weeks, the areas of wounds were found as 4.25, 3.33, 4.01 and 3.43 mm² in group 1 (standard, FSC), group 2 (SDH treated), group 3 (SPH treated) and group 4 (TYH treated) respectively. The group 5 (untreated control) showed a decrease in the wound with 4.73 mm² of area owing to the natural phenomenon of healing process. The results are summarized in Table II and Fig. 4. The wound healing activity in chemical induced burns was found to be in the order of SDH > TYH > SPH > FSC > control. The results indicated that the three types of honey used in the study were found to possess significant wound healing activity compared to that of the standard. Interestingly, all the types of honey were found to have better wound healing activity than that of commercial products indicating the superior potential of natural products over synthetic ones. After completion of 38 days it was observed that the wound was cured among all rabbits. The statistical treatment of data was done using student’s t-test and the values were shown in Tables I and II. The data containing t-test were compared to those of standard and control (p<0.05) indicated that there was no significant difference exists between these values. However, among the data of three tested honeys compared with those of the controls, it was found that there was a statistically significant reduction in the wound area of experimental models. The possible mechanism of the wound healing activity of honey could be due to the inhibition of prostaglandins (Al-Waili and Boni, 2003) and by thrombin-induced oxidative burst in phagocytes (Ahmad et al., 2009). In addition, the mild acidity and low-level hydrogen peroxide release, both aided tissue repair and could have contributed to the antibacterial activity of honey resulting in the healing of the wound (Lusby et al., 2005; Visavadia et al., 2008). The wound healing activity of honey could also be due to modulation of the activity of monocytic cells to repair the wounded tissue by releasing anti-inflammatory cytokines and growth factors (Tonks et al., 2003; Henriches et al., 2006).

Among the different types of the honey SDH was found to possess higher healing rate of wounds induced by thermal and chemical methods. However, in thermal induced burns, both TYH and SPH have shown similar wound healing activity but better than that of standard drugs.

Table I: Effect of different types of honey on wound healing activity of thermal burns.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Average area of wound (mm²)</th>
<th>Student's t-test values</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st day</td>
<td>1 week</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Control</td>
<td>4.81 (±0.07)</td>
<td>4.83 (±0.08)</td>
<td>4.54 (±0.06)</td>
</tr>
<tr>
<td>Standard</td>
<td>4.86 (±0.08)</td>
<td>4.79 (±0.06)</td>
<td>4.49 (±0.11)</td>
</tr>
<tr>
<td>SDH</td>
<td>4.78 (±0.06)</td>
<td>4.64 (±0.03)</td>
<td>3.79 (±0.08)</td>
</tr>
<tr>
<td>TYH</td>
<td>4.75 (±0.11)</td>
<td>4.68 (±0.08)</td>
<td>4.24 (±0.09)</td>
</tr>
<tr>
<td>SPH</td>
<td>4.74 (±0.09)</td>
<td>4.89 (±0.07)</td>
<td>4.31 (±0.12)</td>
</tr>
</tbody>
</table>

*Values are mean ± S.E.M. (area reduction). p < 0.05. S=significant, NS=not significant.

Table II: Effect of different types of honey on wound healing activity of chemical burns.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Average area of wound (mm²)</th>
<th>Student's t-test values</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st day</td>
<td>1 week</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Control</td>
<td>5.67 (±0.09)</td>
<td>5.65 (±0.05)</td>
<td>5.45 (±0.10)</td>
</tr>
<tr>
<td>Standard</td>
<td>5.65 (±0.07)</td>
<td>5.6 (±0.04)</td>
<td>5.36 (±0.11)</td>
</tr>
<tr>
<td>SDH</td>
<td>5.61 (±0.10)</td>
<td>5.53 (±0.12)</td>
<td>5.09 (±0.09)</td>
</tr>
<tr>
<td>TYH</td>
<td>5.66 (±0.05)</td>
<td>5.53 (±0.08)</td>
<td>5.06 (±0.11)</td>
</tr>
<tr>
<td>SPH</td>
<td>5.64 (±0.12)</td>
<td>5.58 (±0.06)</td>
<td>5.24 (±0.07)</td>
</tr>
</tbody>
</table>

*Values are mean ± S.E.M. (area reduction). p < 0.05. S=significant, NS=not significant.

Fig. 1: Untreated (A) thermal and (B) chemical induced burns.
Fig. 2: Thermal burns after 38 days treatment with (A) Sidr honey, (B) Thyme honey and (C) Spring honey.

Fig. 3: Wound healing effect of different types of honey on thermal burns.

Fig. 4: Wound healing effect of different types of honey on HCl induced burns.
CONCLUSIONS

It was concluded that honey in general could be employed as topical wound healing agent and was also proved that SDH, SPH and TYH honeys could be used as natural wound healing agents besides commercial synthetic analogs tested in the study. Further the present investigation established that SDH was possessing better wound healing activity than that of TYH and SPH.

ACKNOWLEDGEMENT

The authors are thankful to the Government Medical Research Center, Zawia, Libya and Research Faculty of Pharmacy, University of Zawia, Libya for providing the necessary research facilities.

REFERENCES


Emsen IM. A different and safe method of split thickness skin graft fixation: Medical honey application. Burns. 2007; 33: 782-787.


How to cite this article: