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# Comparison of Manuka Honey (Manuka Nd, G) and Etacridine Lactate (Rivanol) Applications in the Treatment of Infected Wounds in Cats

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**ABSTRACT**

***Background*:** Ethacridine lactate (Rivanol) has been used as an antibacterial drug in the treatment of infected wounds for many years. Although Manuka honey has been used in the treatment of burns, ulcers and infected wounds in human medicine for many years, its use in veterinary medicine is new. Manuka honey has been found to provide rapid cicatrization and lower chronic pain levels, to prevent bad odor, and has antibacterial properties. The aim of this study was to compare the effects of Etacridine lactate and Manuka honey in the treatment of infected wounds in cats.

***Materials, Methods & Results*:** In this study, 32 cats, with infected wounds in different areas on their body, were used. Cats were divided into two groups. The Rivanol group (n = 16) consisted of 6 female and 10 male cats aged 4 ± 3 years from different breeds and in several weights. Manuka group (n = 16) consisted of 7 male and 9 female cats of different breeds and weight and aged 4 ± 2 years. Rivanol was applied to the first group and Manuka honey (Manuka Nd, G) was applied to the second group. First measurements were recorded after the surgical debridement of the wound area. Four measurements were made every 3 days. The size (length - width) of the wounds was measured and recorded. Parenteral Marbofloxacin was administered orally in all cases. In order to prevent the contact of the cases with the dressing, the collar was worn. In the Rivanol group, when the first measurement values (length: 4.29 ± 2.78 cm, width: 2.13 ± 0.58 cm) and the 4$^{th}$ measurement values (length: 2.21 ± 1.37 cm, width: 1.06 ± 0.41 cm) were compared, there was a decrease in the wound size. In the Manuka group, when the first measurement values (length 2.84 ± 1.51 cm, width: 2.01 ± 1.03cm) and the 4$^{th}$ measurement values (length: 1.42 ± 1.10 cm, width: 0.90 ± 0.72cm) were compared, the wound sizes were diminished as in the Rivanol group. In all measurement days, the differences between of Rivanol and Manuka groups concerning the width, length and wound sizes were not statistically significant ($P > 0.05$). Wound size, length and width showed a linear decrease over the measurement days. These decreases were similar in Rivanol and Manuka group. There was no statistically significant difference between Rivanol (12.44 ± 3.74 days) and Manuka (12.44 ± 4.68 days) groups over the cicatrization period ($P > 0.05$).

***Discussion*:** Rivanol and Manuka honey were effective in wound healing. Although there were no differences between the two groups, the wound sizes decreased in each measurement of the wounds. A moist environment was formed on the wound, debrideman accelerated and granulation tissue formation was encouraged with the application of both topical agents. Therefore, it was considered that wound healing in our cases was successful. It has been found that honey is frequently applied in wound treatment and in many areas in human medicine. However, in the field of veterinary medicine, there were few investigations. In the treatment of infected wounds of cats, it was determined that the application of Rivanol and Manuka honey yielded similar results in terms of time and there was no statistically significant difference. Manuka honey was found to be an alternative to Rivanol in the treatment of infected cat wounds. Manuka honey preparations (pad or pomade) were preferred because of the ease of use. In order to determine the efficacy of manuka honey in wound healing, it was thought that many further clinical or experimental studies should be carried out using microbiological, biochemical and histopathological parameters.

**Keywords:** cat, infected wound, manuka honey, etacridine lactate.

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## INTRODUCTION

A 0.01% Ethacridine lactate (Rivanol) solution is a preferred antiseptic solution [11]. It acts by binding to DNA of Bacteria. It is especially effective against Gram (+) bacteria. It is also effective in the presence of organic substances such as purulent matter, blood and serum [15].

Honey has antibacterial effect and many other therapeutic properties supporting healing [4,7,8]. Honey creates a cleansing effect on the wound and debride the necrotic tissue. It protects the moist wound and reduces the infection. It promotes formation of granulation tissue. It provides epithelialization on wound surface [5,19]. Many previous literature have suggested that honey can be used as a dressing for ulcers, burns and skin ulcers [13,24].

Manuka honey is a topical agent that provides rapid healing, controls malodour, has antibacterial properties and lower chronic pain levels. Manuka honey containing membranes have been reported to have a high level of antibacterial effects against bacteria causing wound infections in animals [9,20].

Manuka honey, native to New Zealand, contains a unique Manuka Factor (UMF), which provides an additional antibacterial agent [14,25,26].

In experimental studies conducted on animals, Manuka honey was found to improve the cure of ulcers, lacerations and burns. Currently, Manuka honey is most commonly used in the treatment of burns as well as venous leg ulcers [10,12,18,27].

Since manuka honey has biological activities such as antioxidant, antimicrobial and antiproliferative, scientists still study on the Manuka honey [21].

The aim of the study was to evaluate the effects of these two topical drugs in the treatment of septic wounds in cats.

## MATERIALS AND METHODS

### *Animals*

The study included 32 cats with different breed, age and sex having infected wounds in their different anatomic areas. Cats were divided into two groups. Rivanol (16 cases) was applied to the first group and Manuka honey (16 cases) was applied to the second group. The Rivanol group (n = 16) consisted of 6 female and 10 male cats aged 4 ± 3 years from different breeds and in several weights. Manuka group (n = 16) consisted of 7 male and 9 female cats of different breeds and weight and aged 4 ± 2 years.

Wound healing was observed and recorded. In this process cats were hospitalized.

In the cases, Rivanol Ointment (0.2% Rivanol Biotechnic®)[1], either Manuka G 15 g Gel (Kruuse®)[2] or Manuka ND 5*5 cm non-adherent dressing (Kruuse®)[2] were applied upon wound. Marbofloxacin (Marbocyl tb P 20 mg, Vetequinol®)[3] was administered orally to all cases as systemic parenteral antibiotic.

### *Clinical findings*

General examination protocols were applied to the cats. Cats with any suspected viral or bacterial systemic disease and orthopedic problems (fracture, dislocations) were excluded from the study. Following the examination, firstly the area where the wound was found, then the material to be applied according to the nature of the cat was decided. Manuka pad was preferred in large surface wounds and Manuka gel or Rivanol pomade was used in smaller or mobile areas.

After the general examination, it was evaluated whether the cat would allow the procedures to be performed. Medetomidine (Domitor, Zoetis®)[4] was applied at a dose of 0.08 mg / kg for sedation to the cats that do not allow the treatment.

The hair of the wound area was shaved. Surgical debridement was performed according to asepsis and antisepsis rules. Then the first measurement of the wound was performed and recorded. The material to be used was selected and wound dressed with rivanol pomade, manuka pad, or manuka pomade. After three days, dressings were opened, measurements were made and the values were recorded. Wound was closed for the measurement three days later. Four measurements were performed every 3 days in all cases. In some cases, measurements continued with 3 days interval. The first 4 measurements of all cases were evaluated for statistical analysis. The values obtained after the 4th measurement in some cases were not included in the statistical analysis.

### *Statistical analysis*

The normal distribution of the data was evaluated by histogram, q-q graphs and Shapiro-Wilk test. Homogeneity of variance was evaluated by Levene test. Friedman test was used for comparisons between mea-

surements in each group, and Mann Whitney U test was used for intergroup comparisons in each measurement.

The effect of Manuka and Rivanol on wound healing time was determined using covariance analysis (ANCOVA) by taking the initial wound size as common variable. Statistical analysis of the data was performed with NCSS 9.0 (NCSS, LLC®)[5] package program. Significance level was accepted as $P < 0.05$.

## RESULTS

Compare to the first measurements, the sizes of the wounds were decreased in the final measurements in both groups, initiation of cicatrization and significant improvements in wound healing were observed (Figures 1 & 2). Descriptive statistics of the wound sizes of animals in groups are given in Table 1 and Table 2.


**Figure 1.** First measurements A1, B1, C1, D1 and last Measurements A2, B2, C2, D2 of Manuka group cases.

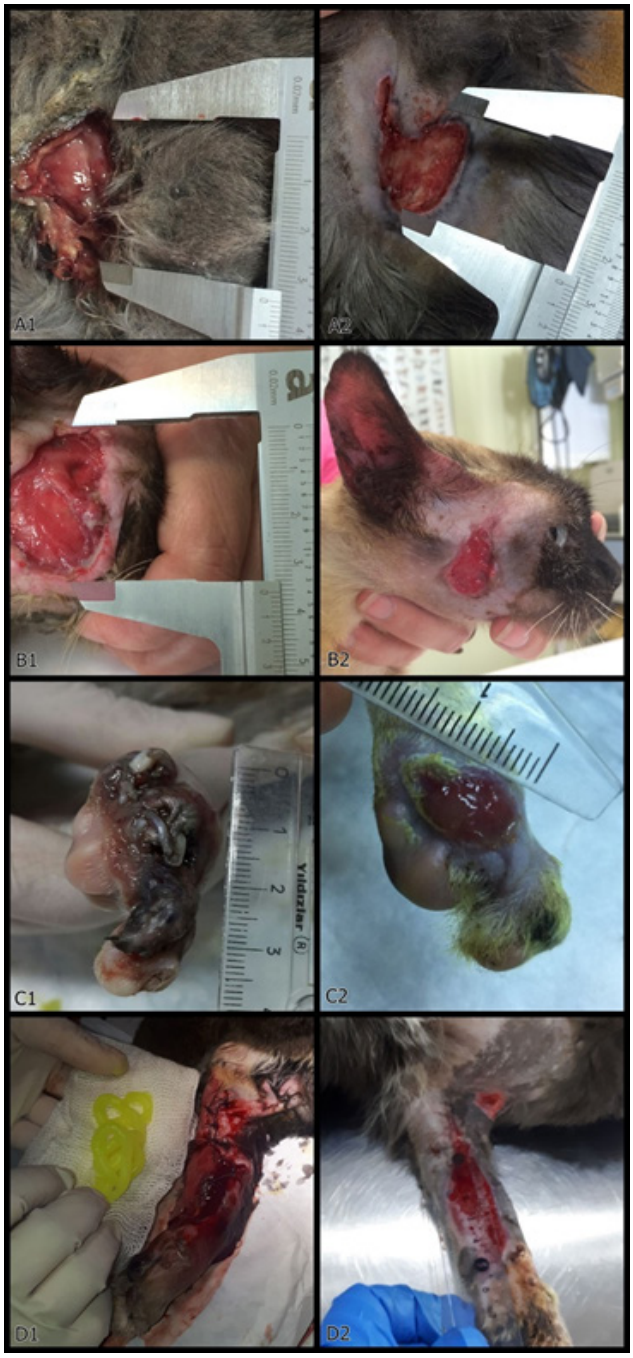


**Figure 2.** First measurements A1, B1, C1, D1 and last Measurements A2, B2, C2, D2 of Etacridine Lactate (Rivanol) group cases.

**Table 1.** Descriptive statistics of wound sizes.

| Group | Wound sizes (Mean ± Standart Deviation) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 1. Measurement | | 2. Measurement | | 3. Measurement | | 4. Measurement | |
| | Length | Width | Length | Width | Length | Width | Length | Width |
| Manuka | 2.84 ± 1.51 | 2.01 ± 1.03 | 2.38 ± 1.50 | 1.61 ± 0.95 | 1.94 ± 1.35 | 1.24 ± 0.85 | 1.42 ± 1.10 | 0.90 ± 0.72 |
| Rivanol | 4.29 ± 2.78 | 2.13 ± 0.58 | 3.56 ± 2.47 | 1.88 ± 0.69 | 2.79 ± 1.64 | 1.41 ± 0.45 | 2.21 ± 1.37 | 1.06 ± 0.41 |

**Table 2.** Descriptive statistics of wound areas.

| Group | Wound areas ($cm^2$) (Mean ± Standart Deviation) | | | | Cicatrization time (Day) |
|---|---|---|---|---|---|
| | 1. Measurement | 2. Measurement | 3. Measurement | 4. Measurement | |
| Manuka | 6.79 ± 6.72 | 4.63 ± 4.98 | 3.08 ± 3.64 | 1.70 ± 2.07 | 12.44 ± 4.68 |
| Rivanol | 9.55 ± 7.54 | 6.76 ± 5.01 | 3.95 ± 2.51 | 2.47 ± 1.83 | 12.44 ± 3.74 |

On all measurements days, the differences between Manuka and Rivanol groups concerning the width, length and wound sizes were not statistically significant ($P > 0.05$) (Table 3). However, the width, length and size of the wounds showed a linear decrease on the days of measurements. These decreases were similar in Manuka and Rivanol groups.

The effect of Manuka and Rivanol on wound healing time was determined by covariance analysis (ANCOVA) by taking the initial wound size as common variable. Covariance analysis is a statistical method used to investigate whether there is a difference between the groups in terms of dependent variable (s) after the effect of the common variable (s) is eliminated. Wound cicatrization time as dependent variable, Manuka and Rivanol group as independent variable, and the first measurement values of wounds as common variable were taken for analysis.

The results of covariance analysis in which the common variable is included in the model are given in Table 4.

In the table of variance source, firstly it is necessary to determine whether the slope of the wound size lines on wound healing time. The interaction between the groups and the wound size was examined in order to check whether the slope of the regression lines is the same in both groups. We investigated whether there is interaction between the groups with the wound size.

**Table 3.** Statistical significance of wound size and area measurements between groups.

| Group | Wound size | | | | *P Values* |
|---|---|---|---|---|---|
| | 1. Measurement | 2. Measurement | 3. Measurement | 4. Measurement | |
| | | | Length | | |
| Manuka | 2.84 ± 1.51[a] | 2.38 ± 1.50[b] | 1.94 ± 1.35[c] | 1.42 ± 1.10[c] | < 0.001 |
| Rivanol | 4.29 ± 2.78[a] | 3.56 ± 2.47[b] | 2.79 ± 1.64[c] | 2.21 ± 1.37[c] | < 0.001 |
| *P Values* | 0.239 | 0.210 | 0.138 | 0.094 | |
| | | | Width | | |
| Manuka | 2.01 ± 1.03[a] | 1.61 ± 0.95[b] | 1.24 ± 0.85[c] | 0.90 ± 0.72[c] | < 0.001 |
| Rivanol | 2.13 ± 0.58[a] | 1.88 ± 0.69[b] | 1.41 ± 0.45[c] | 1.06 ± 0.41[c] | < 0.001 |
| *P Values* | 0.171 | 0.094 | 0.171 | 0.160 | |
| | | | Wound area | | |
| Manuka | 6.79 ± 6.72[a] | 4.63 ± 4.98[b] | 3.08 ± 3.64[c] | 1.70 ± 2.07[c] | < 0.001 |
| Rivanol | 9.55 ± 7.54[a] | 6.76 ± 5.01[b] | 3.95 ± 2.51[c] | 2.47 ± 1.83[c] | < 0.001 |
| *P Values* | 0.119 | 0.128 | 0.160 | 0.128 | |

[a,b,c]The difference between measurements with different letters on the same line is statistically significant.

**Table 4.** Analysis of covariance on wound cicatrization time in groups.

| Source of Variance | Sum of Squares | df | Mean Square | F Values | *P* Values |
|---|---|---|---|---|---|
| Corrected model | 17.102 | 3 | 5.701 | 0.307 | 0.820 |
| Intercept | 2160.254 | 1 | 2160.254 | 116.149 | < 0.001 |
| Groups (Manuka/ Rivanol) | 9.841 | 1 | 9.841 | 0.529 | 0.473 |
| Wound area (1. Measurement) | 0.500 | 1 | 0.5 | 0.027 | 0.871 |
| Groups x Wound area | 15.742 | 1 | 15.742 | 0.846 | 0.365 |
| Error | 520.773 | 28 | 18.599 | | |
| Total | 5488.0 | 32 | | | |

df: Degree of freedom. $R^2$ (Determination Coefficient): 0.32.

According to ANCOVA results, after the correction of effect of wound size on wound healing period, the effects of Manuka and Rivanol were not statistically significant (P = 0.473).

After correcting effect of the wound size (Corrected wound size = 8.17), the descriptive statistics of Manuka and Rivanol groups for cicatrization periods are given in Table 5.

There was no statistically significant difference between Manuka and Rivanol use in the treatment of wound concerning the cicatrization time, and Manuka honey could be used as an alternative to Rivanol.

**Table 5.** Descriptive statistics of cicatrization time in groups after correction of wound area effect.

| Group | Cicatrization time (Day) (Mean ± SEM)* | |
|---|---|---|
| | Real | Adjusted |
| Manuka | 12.44 ± 1.17 | 12.55 ± 1.10 |
| Rivanol | 12.44 ± 0.94 | 12.60 ± 1.09 |

*Group mean and standard errors adjusted according to wound area = 8.17 cm2

## DISCUSSION

Moisture is the best healing medium in a wound. Autolytic debridement is accelerated in tissue in a humid environment and granulation tissue formation is promoted, epithelization is faster [4,11]. Our results showed that Rivanol and Manuka honey were effective in wound healing. Although there were no statistically significant differences between the two groups, it was seen that the wound size was reduced in every measurement. With the application of both topical agents, a humid environment was formed on the wound, debridement accelerated and granulation tissue formation was encouraged. This led to a successful cicatrization.

The wound should be cleaned to eliminate the infection. For this purpose, debridement, antiseptic solutions and pomades providing the cicatrization or alternative medications (such as honey, acemannan, and aloe vera) are used [11]. The wounds in all our cases were characterized as septic wounds. In our cases, cleansing was performed, hemostasis was achieved and debridement was performed. The sizes of the wounds were measured. Significant improvement was observed in the wounds in the final measurement of the cases. It was determined that Manuka and Rivanol were topical agents to prevent infection in wounds and could be applied in septic wounds.

When wound care is done with Manuka honey, gloves should be used and normal aseptic techniques should be adopted. Normal treatment procedures should be followed. Cleaning should also include surgical or physical debridement under sedation [25,26]. Asepsis and antisepsis rules were applied at the highest level during the wound care of our cats. Attention

was paid to use sterile dressing materials. It has been determined that compliance with asepsis and antisepsis rules and debridement process are extremely effective in wound healing and give successful results in infected wound treatments. When Manuka honey was applied to aggressive cats, sedation was achieved with Medetomidin. These hard-tempered cats were street cats.

Parenteral antibiotic treatment is also preferred in the treatment of septic wounds and veterinary surgery. In recent years, use of marbofloxacin preparations has been seen [23]. However, attention should be paid to high doses in antibiotic use [1]. In this study, Marbofloxacin was used in all cases. Co-administration of topical and systemic antibiotic drugs in infected wounds positively affected wound healing. In a case report, Akın et al. [1] reported high doses of Marbofloxacin causing acute blindness. No complications were encountered in the dose we used in our study. Therefore, use of 2 mg/kg/day of Marbofloxacin was effective for the treatment of septic wounds of cats.

The development of wound care products including honey is continuing rapidly. It is used in wound dressings or in tube form for wound treatments [7,8]. Manuka honey is scientifically recognized for its antimicrobial and wound healing properties and is now used in topical treatment of wound infections in clinics [17]. Manuka honey adsorbed pad form and pomade form were applied in our cases (Manuka G 15 g Gel Kruuse and Manuka ND 5*5 cm non-adherent dressing Kruuse®)2. It has been found that honey is frequently applied in wound treatment and in many areas in human medicine. However, in the field of veterinary medicine, to the best of authors' knowledge there are few investigations.

It has been observed that dressing with honey reduces odor in infected wounds. There are many literatures suggesting that honey can be used effectively as a dressing for wounds, burns, and skin ulcers [5,6,9,20,21]. Not all honeys have the same effect. Only use of medicinal honey is recommended [11]. In our study, Manuka honey, which is a medicinal honey and which has been used in wound treatment in recent years, was used. The debridement and antibacterial effect of Manuka honey in wounds were determined in our study. None of our Manuka cases experienced bad odor during dressing changes.

Honey creates a humid environment for optimum healing conditions. Honey forms a diluted honey film under the dressing, which prevents the dressing from adhering to the wound bed. There is no watering and pain in the newly formed tissue during the dressing change [16]. It was observed that the dressing material did not adhere to the wound and there was no watering on the wound during the changing of dressings of the cases in Manuka group. However, some of our cases showed signs of pain during dressing changes. This pain was attributed to the cat's temperament. For this reason, dressing change was performed under sedation in some cases. However, in order to determine the effects of Manuka honey, more comprehensive and comparative studies should be performed in experimental and clinical cases.

It has been reported that application of 4% topical Manuka honey had no toxic effects in chinchillas with chronic rhinotracheitis and chronic otitis cases [2]. Manuka honey has been found to be effective in the treatment of rosacea (rose disease) in humans. It has been concluded that honey is a biologically active and clinically interesting substance, but more research is needed for a comprehensive understanding of the medical value in dermatology [17]. Honey was found safe and effective. It stimulate wound healing in the treatment of Exomphalos major (infant hernia, abdominal cleft) [22]. It has been suggested that Manuka honey can be used in bone tissue regeneration [14]. Honey has been reported to be preferable in aphthous stomatitis and other oral lesions, especially those with ulceration and inflammation. Manuka honey is used successfully in mouth odor [5]. In literature, Manuka honey is a popular topical agent in recent years, and it can be applied in areas where the inflammation occurred. Although Manuka honey is used in many areas of human medicine and many scientific studies are being performed, it was observed that the use of this agent in veterinary medicine is new and there was not sufficient scientific study. In this aspect, we believe that our research will contribute to the field of veterinary medicine. More research is needed on the use of honey in wound healing.

In a study, a 17-month-old male great danua with a wound on his leg that had been bitten by another dog, was bandaged by dressing with a medical honey pad for 2 weeks, and it was determined that epithelization increased each time the bandage was opened [16]. On the other hand in our study, Manuka adsorbed pad was used in Manuka group. The dress-

ing was repeated 4 times with three days intervals and it was determined that epithelization increased in each bandage change.

In a previous study, Manuka honey and Manuka gel were applied to compare wound healing in experimentally formed wounds in the metacarpal region of 10 horses. A 2x2 cm wound was formed on both metacarpal of the five horses and was contaminated with horse stool for 24 hours. The wound of the other 5 horses was kept sterile and not contaminated. It was determined that wounds contaminated with feces were healed faster than non-contaminated wounds [3]. Rivanol group was the control group of our study. The efficacy of Rivanol in wound healing has been known for years. Studies on Manuka honey are limited. In both of our groups, wound healing occurred rapidly and no statistical difference was determined in terms of cicatrization times.

## CONCLUSIONS

It was determined that application of Rivanol and Manuka honey in the treatment of infected wounds of cats give similar results without statistically significant difference in terms of cicatrization time. Manuka honey was found to be an alternative to Rivanol in the treatment of infected cat wounds.

Rivanol, a yellow chemical preparation, has difficulty in its use due to its staining property and sharp odor. Therefore, it can be suggested that Manuka honey preparations (pad or pomade) are preferable because of the ease of use.

It was concluded that many clinical or experimental studies should be performed by using microbiological, biochemical and histopathological parameters in order to determine the efficacy of Manuka honey in wound healing.

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