Ʉȁ ʹȴɄȽȵʹ ¢ ʐ ȽȸɃ Ū ȴȵȵȁ ȿ Ƚȁ ȵ

Ȼɢɞǝ Ů ɤůŰɋɛɩ ɜ ɡɔŮŬɉ

ȼɛɐɛ Ŭɖɶɞɢɋɛ ŮŬɉ & ɖɶŰŮɜɞǝɞɔŬɉ

ʐ ȴȿ ȴȼ ¢ ȼ ¢ ȵ ȁ ʹȼ Ƚɖȁ ȶȼ ¢ ɅȽȁ ȶ¢ ȵ ɸɅȁ ȵ¢ ȵ ʐ ȴȿ Ƚɋ ʹ

ȼ ¢ ȵ ɄȴɅȽȸɉ ¢ ȵ ȼ Ƀ Ɉ Ƀȿ Ɉ ʐ ɄȸɈ ȴʹ ȁ ʹ ȼ Ƚ

STAPHYLOCOCCUS AUREUS* ȶȁ Ƚ *PSEUDOMONAS AERUGINOSA

STUDY OF THE ANTIMICROBIAL ACTIVITY OF HONEYS PRODUCED IN OLYMPUS REGION AGAINST *STAPHYLOCOCCUS AUREUS* AND *PSEUDOMONAS AERUGINOSA*

ȼ ȵȁ ɸ¢ ȿ ȁ ɉ ɅȽȵȼ Ƚʹ ȁ

ȿ ȁ ɅȽȵȁ 2015

ɀ Ůờɏűɖ űɖɠŬɜűɷŬəűɖɟ ɘŬəɐɠŭɟ Ÿůɖɠɛ Ůờɑ ɜ űɖɠ´ Ůɟ ɞɜɢɐɠűɞɡ Ƀəɨ ɛ´ ɞɡ ɏɜŬɜűə
Staphylococcus aureus əŬə*Pseudomonas aeruginosa*

¢ɻɜɛŮɔ▸ɐƈƒƎɑɛɓɐɡɔ▸ŮɡŰɔɔɐ Ⱥ´ɔŰɻɛ´ɐ

Ⱥ´ɔɓɔ▸ý ɤɜ: **ɀ ɦjůɹɔŮɔ▸ɐƈƒ qɒ[ɛɐŰɻɜɛɡƒ:** Ⱥ´œɐɡɻɐƈƒ ɔŮƈƒɖɔɖŰéɡƒ ɖɜɛŰŰ‰ɜɐɔ▸ɐɔɖŮƒ ɀ ɜɔɻɐɓɔɤɜ Ű‰g ¢ɛɐɛŰŰ‰ɡƒ ɖɜɛɡɖɛůɖŮƒ & ɖɜɛŰŰ‰ɜɐɔ▸ɐɔɖŮƒ Ű‰g Ⱶ▸ŮɔŮ ɜůŰ[ɛœg ŪŮůůŮ▸ɖŮƒ.

ɀ ŮɻɔɐɡɔɐŦŰ‰ɡƒ Ⱶ▸ŮɔŮ▸ɜɹ Ű[ɡƒ: TŮƈƒɖɔɖŰéɡƒ Ⱥűŭɻɛɐůɛɣɜɖɡƒɀ ɜɔɻɐɓɜɛɐ▸ɐɔɖŮƒɛŮɣɛűŭůɖ ůŰ[ɖ ɖɜɛŰŰ‰ɜɐɔ▸ɐɔɖŮ Ű‰g Ű£ɐɛŰŰ‰ɡƒ ɖɜɛɡɖɛůɖŮƒ & ɖɜɛŰŰ‰ɜɐɔ▸ɐɔɖŮƒ Ű‰g Ⱶ▸ŮɔŮ ɜůŰ[ɛœg ŪŮůůŮ▸ɖŮƒ

ɻ ɛɐɨ Ű‰ɔŮƒũɻ ɖɔɦɻɜɛɡƒ: Ⱥ´œɐɡɻɐƈƒTŮƈƒɖɔɖŰéɡƒɖɜɛ´ɔɖɻɐűɐɻɜɔɐɡƒůŰ[ɖ ũŮɜɤɛɜɔɐ Ű‰g Ű£ɐɛŰŰ‰ɡƒ ɖɜɛɡɖɛůɖŮƒ& ɖɜɛŰŰ‰ɜɐɔ▸ɐɔɖŮƒŰ‰g Ⱶ▸ŮɔŮ ɜůŰ[ɛœg ŪŮůůŮ▸ɖŮƒ

Ágc Ůɟ sůŰdůf

Ágc Ůɟ sůŰí Ű ɜ Ů ɦ ə ý ɜ Ű Ű ə Ű d ɔ d Ű ɛ g, ə. ɀ ɦ ů ů s Ů ɔ ɐ q d ɛ ɐ Ű ɟ s ɐ ɔ s Ů Ű ɜ Ɣ Ɣ ɛ ɔ d ůg ɜ Ů ɟ ɔ Ű ů d Ů ə Ů ɔ Ű Ű ɜ ůg ɜ Ů ɛ ɐ ə Ű d ɛ ŭ ɐ ɔ d ů d.

Á ´ ɔ ´ ə ɔ ɣ ɛ ɜ, Ů ɔ ű ɟ Ɣ ɛ ɤ Ű ɡf Ů g c Ů ɟ sůŰdůf ɛ g ə Ů ɔ ů Ű Ű ɛ ɣ ɔ d Ű d ɡf Ů ɔ Ű ɟ ɛ ´ ɐ ɡf ə. ɀ Ů ɟ ə ɛ g ə ɔ Ɣ Ű ɛ Ч Ů Ɜ ɔ Ů ɔ ɜ Ű d ə Ů ɔ ə. ɟ ɛ ɛ i Ű ɛ ɔ Ú ũ ɟ d ɔ ɦ ɟ s ɐ.

¢ ɣ ɔ ɛ ɡf d Ů ɐ d Ů ɔ ɜ Ů ɜ Ů g c Ů ɟ sůŰ é ů ɤ ɦ ə d Ű d ɜ ɛ Ɣ ũ Ů Ű ɛ g Ů ɟ ɔ Ů ů Ű d ɟ ɐ ɛ g, ɔ ɔ Ů Ű d ɜ Ɣ ɟ sůŰd ůg ɜ Ů ɟ ɔ Ů ů d Ů ə Ů ɔ Ű ɛ ű ɔ ɔ ɔ ɦ ə ɔ ɐ Ů ´ ɛ g Ů ɔ Ů Ű ɛ c d d ə Ů Ű d ɜ ůg ɜ Ɣ ũ Ů ɔ ű ɦ ɛ g ¢ ɛ ɐ ə Ů Ч Ů ɟ Ů ů ə Ů g ɐ ɔ s Ů Ű d ɜ ɓ ɛ ɐ d Ů Ɣ Ű d ɡf ə Ů ɔ Ű d ɜ ɛ ɔ ɔ ɣ ɔ Ů Ɣ ɛ g ɔ ɔ Ů Ű d ɜ ů Ű ɟ ɔ ɔ d ´ ɛ g ɛ g ´ Ů ɟ Ů c Ů ɔ.

ɄȺɅȾȺĵ Ƀɀ Ⱥʔ ȷ

III. ȷ ɄɃɇȺȘ ȺɆȤ ȷ ɇȷ

IV. ɆɈȻ¢ ɇ¢ Ɇ¢ ï Ɇɉ ɃȘ Ɉ Ɇȥ ɃɆ

V. ɗɈɗȘ ɈɃ ũ Λȷ ũ Ɉ

[illegible]

[illegible] (Abdelmalek et al. 2012).

[illegible] (*Apis mellifera*), [illegible] (Carnwath et al. 2014). [illegible] (Abdelmalek et al. 2012, Kwakman et al. July 2010).

[illegible] (*Apis mellifera*) [illegible] (Mundo et al.,2004). [illegible] (Voidarou C. et al, 2011).

[illegible] *Staphylococcus aureus* [illegible] *Pseudomonas aeruginosa*. [illegible] Manuka 25+ (Manuka Health) [illegible].

[illegible] 2 in vitro [illegible] (*wells diffusion method*) [illegible] (*Minimum Inhibitory Concentration, MIC*) [illegible] (*mircotiter plates*). [illegible] MIC [illegible]

[illegible] (Anthimidou and Mossialos 2012).

[illegible] *S.aureus*. [illegible] *S. aureus* [illegible] Manuka 25+ [illegible] (MIC 3,125% v/v) [illegible] Manuka 25+ (MIC 6,25% v/v).

[illegible] *P. aeruginosa,* [illegible] *P. aeruginosa* [illegible] Manuka [illegible] (MIC 6,25% v/v), [illegible] Manuka 25+ (MIC 12,5% v/v).

[illegible] *S. aureus* [illegible] (MIC) [illegible] Manuka 25+. [illegible] MIC [illegible] MIC [illegible].

[illegible] *P. aeruginosa*, [illegible] (MIC) [illegible] Manuka 25+. [illegible] MIC [illegible] MIC [illegible].

Abstract

In recent years, human pathogen organisms have developed resistance, as a response to the indiscriminate use of antimicrobial agents, which are commonly used to treat infectious diseases. For this reason, it is essential to find alternative antimicrobial strategies and so this situation has lead to reassessment of the therapeutical use of traditional treatments, such as plants and their products, because they can be a source of many active ingredients that exhibit multiple therapeutic properties and additionally constitute models for the synthesis of a large number of drugs.

Substances that are produced by bees (*Apis mellifera*), including propolis, honey, wax and poison, have been used for their medicinal properties throughout history. The application of honey in medicine has been abandoned with the advent of antibiotics but recently has been "rediscovered" and increasingly gained acceptance, because studies show that it consists of an effective antibacterial agent for the treatment of ulcers, wounds, and other epidermal infections.

Both in Greece and worldwide, honey has been used for centuries as a food preservative as well as a treatment for diverse health problems. The geomorphology and variety of flora, gives the opportunity to bees (*Apis mellifera*) to produce a wide variety of honeys from pine and citrus trees, thyme or other floral origin, which gives the finished product its own specific sensory properties. Despite the variety and recognized quality, little research has been done about the antibacterial properties of Greek honey.

Aim of this study was to evaluate the antibacterial activity of nine Greek honeys produced in Olympus region, against two major nosocomial pathogens that are involved in the majority of wound infections, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The samples had been compared to Manuka honey, which is known for its strong antimicrobial activity and to an artificial honey made in the laboratory.

In total, all nine honey samples were evaluated using two in vitro methods: a) *wells diffusion method* and b) determination of the *minimum inhibitory concentration (MIC)* in *microtiter plates*. Research for antibacterial mechanisms was performed by adding catalase, which degrades H_2O_2 and proteinase K, which inactivates proteins or oligopeptides that are found in honey thus contributing to its antibacterial activity.

All nine honey samples demonstrated antibacterial activity against *S.aureus.* Six out of nine have shown significantly larger inhibition zones compared to Manuka honey and four of them demonstrated lower minimum inhibitory concentration value (MIC 3,125% v/v) than Manuka honey (MIC 6,25% v/v)

Regarding *P.aeruginosa*, all nine honey samples demonstrated antibacterial activity against this bacterium. Eight out of them have shown significantly larger inhibition zones and all of them demonstrated lower minimum inhibitory concentration value (MIC 6,25% v/v) compared to Manuka honey (MIC 12,5% v/v).

As for the antibacterial mechanisms against *S. aureus*, four out of nine honey samples, which have shown better antibacterial activity than Manuka were examined. All four honeys demonstrated antibacterial activity due to generation of H_2O_2 because when catalase is added, their MIC was increased. Two out of four are possible to contain antibacterial proteins or oligopeptides contributing to their antibacterial activity, since when they were treated with proteinase K their MIC was increased.
Regarding *P.aeruginosa*, the test was carried out for all nine samples, because, all of them have been proven to demonstrate antibacterial activity due to generation of H_2O_2, because when catalase was added their MIC increased and five out of nine honeys demonstrated antibacterial activity which could be attributed to proteins or oligopeptides, because when proteinase K was added the MIC increased.

Ł ŪÆq Λ¢ ¢ ĦΓB z ÆΛBÆ

1. Æsůŭɔɐ

1.1 ¢ ɘ ŮʁBŭɔ ɛ yəəs:

z yəɘ ůi ɛűʏ ɜŭ ɛŮŰłɜ ɜɛɛɑdŮůɑdŭ ŮʁBŭɜ ñ Ű ɔəgəɦ ´ɟɛɑɦɜ Ű ɛ´ɛœ ´ŭɟ Ɣɔɛgɜ ɛɘ ɛyəəsůůŮʃ (*Apis mellifera*), əŭɑı ʃ ůgəəəyɔɛgɜ, ɛŰŰŭʃ y´ ɛgɜ əŭɔ Ŭ ɛɑdqəůɛgɜ ůŰɦʃ əqɟ ɐqɟ ŮʃŰ ɛgʃŰ ɜyəŰŭʃ əŭɔ ƔəəɛggʃűgŰəɛi ʃ gɛɛi ʃ Ŭ ɦ ŭsƳűɛɟ Ŭ ɛʏ ɜŰŭɔƳ ɛyɟ qŰ ɛg űgŰɛi ò. Æœŭɔ ɛsŭ ɔəgəsƳ, əɛəəı ŭdʃ ɛgůɑŭ´ɛg ´ŭɟ ƔɔŮŰŭɔ Ŭ ɦ ɛyəəsůůʃ ɛŮŰƳ Ű ůgəəəɔɐ ɜyəŰŭʃ ɐ űgŰəəı ɜ ůəəɟɑůŮʏ ɜ ´ɛg ´ɟɛəŭəɛi ɜŰŭɔ Ŭ ɦ Ű ɜ əŭŰŭůŭɟ ɛűɐ Ű ʏ ɜ űgŰí ɜ Ŭ ɦ yɜŰɛɛŭəŭɔ ɛɜɛɛƳɛɛɜŰŭɔ ɛŮəəsŰí ɛŮŰŭ (Henriques et al. 2010). ¢ ɛ ɛyəəɔ ŭŮɜ əŭŰłɔɛɟ sɛ´ɛsůdŰŭɔ ůŰŭ Ŭɟ ɦűɛŭ, ŬəəƳ ŭɜŭűyɟ ŮŰŭɔ ʏ ʃ űgůsəɐ ɔəgəəƳ ɛgůɑŭ (Ūɟ Ŭůgɓɛiəɛg et al. 2002).

Ƀɔɛyəəsůůʃ ɛŮŰŭɟ y´ ɛgɜ Ű ɜyəŰŭʃ ůŮɛyəəɔ ɛŮŰłɜ ´ɟɛůdɐəqŮəɛi ɛʏɜ Ŭ ɦ Ű ggʃ ůsŮəɔɔɦɜɛggʃ əŭɔ Ű ggʃ g´ɛűŭɟ gɔɔɔəɛi ʃ Ŭűyɜŭʃ Ű ggʃ əŭɔ Ű ɛɟ qůɛɛ´ɛsɛi ɜ ɔəŭŰłɜ əƳəgɣqŰʏɜ ŭŮəŭəı ɜ Ű ggʃ ŭŮəŭəı ɜ ɦŰŭɔ ŭŮəi ɜŭŰŭɔɜŭŰɟ ŭűɛi ɜ Ŭ ůgdŮůŭʃ Ŭ ɦ Ű ɜyəŰŭʃ. ¢ əgɟ dŭɟ ɛqɟ ɛqɛəəɐ ɛŮŰŭɟ ɛ´ɐ ´ɛg əŭɛɓƳɜŮəɔ ɢı ɟ Ŭ əŭŰƳŰłɜ ɛŮŰŭɟ ɛ´ɐ Ű ɛg ɜyəŰŭʃ ůŮɛyəəɔ ůsŭəɔ Ŭ ɔɟ ŭűɦɛɟqůɟ Ű ɛg ŭəɛŭɛŭɟ dŰłɟ ůɛgəəɟ ɦɛɔɟ ůŮɔəgəɦɛɔɟ əŭɔ űɟ ɛgəŰɦɛɔɟ. ¢ ɛ ɛyəəɔ Ůɛ´əɛgŰœɛŮŰŭɔ ɛŮʏɜɛgɛŭ Ŭ ɦ Ű ggʃ ŭűyɜŮʃ Ű łʃ ŮʃɔƳgɛŭ ɛyəəsůůŭʃ, Űŭɔɛ´ɛdŭ ɛŮŰŭɔɛəœɛgɜ ŰŭůƳəɢŭɟŭ (Anthimidou and Mossialos 2012).

Ƶŭdı ʃ ŮʁBŭɔ Ű ɛɦɜɛ ŭəŭdyůɛɛ űgůsəɦ ɔəgəŭɜŰəɦ, ŬəəƳ əŭɔ ůɖɛŭɜŰəɐ ´ɖɔɐ gŭŮŰŭɜdɟƳəʏɜ, Ű ɛyəəɔ ɐŰŭɜ ɛəŭ ůɖɛŭɜŰəɐ Ű ɟ ɛűɐ ɔəŭŰɛɜ Homo sapiens Ŭ ɦ Ű ɜŮəɑɛɖɛƳ Ű ɛg. ¢ ´ɟı Ű łʃ ɔɟ Ŭ Ű ŭɐ Ŭɜŭűɛɟ Ɣ ɔəŭ Ű ɛ ɛyəəɔ ůŮ ʏɜŭɔ ŭɑůəɛ Ű ʏɜ Æɛgɛ Ůɟ ɑʏɜ ´ɛg gɟ ɛɜɛəɑɔŮůŰŭɔ Ŭ ɦ Ű ɛ 2100-2000 ´.j ., Ŭɜŭűyɟ Ůəŭł gɟ ɐůd Ű ɛg ʏɖ ű Ɣɟ ɛŭəɛ əŭɔ ʏɖ Ŭəɛsűɐ. ÆŰ ɛggʃ ´Ůɟ sůůɦŰŭɟ Ůʃ Ŭɟ gŰɑggʃ ´ɛəəŭůɛɛi ʃ Ű ɛ ɛyəəɔ gɟ qůsɛɛ´ɛsɛdɖəŮŰɦůɛ ɔəŭ dɟ Ů Ű ɐɛi ʃ ɦůɛ əŭɔ əŭŰɟ səi ʃ ůəɛ´ɛi ʃ, ʏɖ dŮɟ Ŭ ůŭ ɔəŭ Ůəŭı ɛŭŰŭ, əŭŰŭɟ ɟ Ɣəŭł, yəəd əŭɔ Ů ɛi əʏ ůd Ŭɟ Ŭı ɛŭŰɛg, Ŭ əƳ Ů Ůəűɐ ´Ŭɟ ɛgůdŭɛŮəŭŰŭ ɟ Ŭɦɜŭɐ ŭɟ Ɣůd əŭŰƳłɜ Ɣɛůd Ůíŭɟ ɛɔɐ Ű ɛg ůŮŭɜɛɜŰɣ ´ədɔyʃ (Alvarez-Suarez et al. 2010).

[illegible] (Moussa et al. 2012). [illegible] (Henriques et al. 2010).

1.1.1 [illegible] :

[illegible] 181 [illegible] (Alvarez-Suarez et al. 2010). [illegible] (18,4%), [illegible] (30,3%), [illegible] (1,3%), [illegible] (12%), [illegible] (0,169%), [illegible] (169 mg / 100 g) [illegible] 17,2% (Voidarou et al, 2011). [illegible] (Ewnetu et al. 2013).

[illegible] (Voidarou et al, 2011).

[illegible] 3,2 [illegible] 4,5. [illegible] (Alzahrani et al. 2012).

[illegible] (Alzahrani et al. 2012).

1.1.2 qpŬŰĵɛűɘɒɐ Ŭɜɑŭɛůɒɘɕi :

¢ ɘŭɘŬɑŰŰĵɑ ůɑɛŬůɑŬ Ű̃ɛg ɛůɒɘɕi ůŰ̃l ŭɘŬŰĵɛűɐ, ɛűůɒɒůŰŰɔ ůŰ̃ɡʃ ´ɛɘɘŬ ɘɣɡʃ űgůɘɕɘɔɛɘɣɡʃŮ ɘŭĵ Ɣůɑɡʃ Ű̃ɛg.

ɸɛ ɛɣɘɘ Ŭ ɛŰ̃ɒůɑŰŰɔ ɘɑgĵɑɤɡʃ Ŭ ɦ gŭŬŰƳɜɑĵ Ŭɔůɡʃ, ´ɛg Ŭ ɛŰ̃ɒɕi ɜ ´Ůĵɑɑɛg Ű̃ɛ 95% Ű̃ɛg ɜɑĵɛi bƳĵɛggʃ Ű̃ɛg. Ŧĵ ɦəůŰŰɔ ɔɘŬ ɣɜŬ ůɔůɡʃůŰɒƳ´ɛɘi´ɘɛɘɛ ɛůɒɛŬ ůŬɔɛƳĵɤɣɜ, ŰŬ ´Ůĵ ɘůůɦŰĵŬŬ ɦ ŰŰɛ´ɛɑŬůɑɔŬɔůŬƳɛŰůŬůŬi´ŮŰ̃l ɛɛĵűɐ ůŰ̃ɛ ɘŮŰɦ ɣɜŰĵɛ. ŦŬŰƳŰ̃l ŭɘŬŭɘɔŰůɑŬ Ű̃l ʃ ɣɣɑdʃ ɛůŰƳ Ű̃l ɜ ´ĵɦůɘɑdɣɑ Ű̃ɛg ɛůɒɘɕi, ɛɘ ɘiĵɘɛɘ gŭŬŰƳɜɑĵ Ŭɔůɡʃ, űĵɛggɘŰɦɛɑ ɘŬɔ ɔɘgɘɦɛɑ, ɔĵɐɔɛĵŬ ɛůŰŰűɣĵɛɜŰŰɔ ůŰ̃ɛ ŬɑɛŬ ɘŬɔ ɛ´ɛĵɛiɜ ɜŬ ɛĵɑůɛɛ´ɛɘɑdɛiɜ ɔɘŬ Ű̃ɡʃ Ű ŬɔŰƳůůɡʃ Ůɔɣĵɔ ůŬɡʃ Ű ɦ Ű̃ɛ Ŭɔɑĵı´ɛɔɛ ůı ɛŬ. ¢ ɛŮĵɐůɘŬ ŭɦůɑd 20 g ɛůɒɘɕi ŭiɜŬŰŰɔɜŬɘŬɒiɣŮɔ´Ůĵɑɛg Ű̃ɛ 3% Ű̃ɤɜ Ű ŬɔŰƳɛiɛůɔɤɜ ɑɛŮĵɐůɘɤɜ ŮɔŮĵɔ ůŬɔŰƳı ɜ Ŭɔŭɒı ɜ Ű̃ɡʃ Ŭɔɑĵı´ɛg (Alvarez-Suarez et al. 2010).

Á´ɵɘɣɛɜ, Ű̃ɛ ɛɣɘɘ´ŮĵɘɣɡůɔɒƳŰŰɛɑůɡʃ, ɛɣŰŰɒɘŬəŬɔɘɡɜɛůŰ̃ɛɡůŰ. ¢ ´ŮĵɘɡůɔŰɘɦŰĵŰƳŰ̃ɛg ůŮƳŰŰɛɑůɡʃ ůɑŬɔɛůɑŰŰɔ ɑɛŬɔɒɜɛůɑɑ´ɛɘɑdɛɑ, ´ŮĵɦɘŬ ŬgŰƳɣɡůɔŬɔɘɡɜůgdŮıƳŰŰɛɑɑd Ŧĵ, dŮŰŰɛɑɑd (ɑb1), ɣɒɛűɘŬɒɑɑd (ɑb2), ´gĵɘŭɛɜɑɑd (ɑb6) əŬɔ ɜɘŰůɑɑd ůŮɛɘɑĵƳ´ɛůɛůŰƳ. ɸŬ ɛŰŰŬɒɘɘƳ ůŰ̃ɛɡůŮŬ Ű̃ɡ ɛůɒɘɕi ůgɛɛŰŰƳɡɛgɜ ůŰ̃l ɘ-ŮŰ̃ɛgĵɔɑŬ Ű̃ɤɜ əgŰŰŰĵɘɒı ɜ ɛŰɛƁĵŬɔı ɜ. ɸŬ ɡɜɛůŰ̃ɛɡůŮŬ ůgɛɛŰŰƳɡɛgɜ ůŮ´ɛɘɑɑŰɡʃ Ɓɡɛgdɛɘɣɡʃ ŬɔŰɒŭĵƳŮůɡʃ ůŰ̃ɛɜ Ŭɔɑĵı´ɡɛ ɛĵɔŬɔɘůɛɦ. Ɛ̃Ű̃ɛ ɛɣɘɘ´Ůĵɘɣɡ ŰŰŰɔ ůɑŭdĵɛgʃ, ɡŬɔəɦɡʃ, ɛŬɔƳɜɛ, əŬɔ´gĵɑd̃ɛ. Á´ůdɡʃ, ´ŮĵɛiůŮɡʃ ŮɑŬɔ əŬɔ ŭƳŮűɛĵŮɡʃ Ƴɔɘ-Ůɡʃɡůdɡʃ ɦ´ɤɡʃ d Ŭɔŭɡɘɛgɛɑiɜd ´ɛg Ŭ ɛŰ̃ɒɕiůɑ Ŭ Ůĵ ŬɑŰŰl Ű̃ɛ ɜŮĵɡʃ ɛŭɘŬɔɒɔŭůŰ̃ɛ Ű̃ɛg ɜŮĵɡʃ ɘɛi ůgůŰɛŰŰɛgʃ. ɸɣɘɛgʃ, ´ŮĵɘɣɡɜŰŰɔŬɛɘɛɜƳŬ ůŮɛɘɛĵƳ´ɛůɦŰŰl Ű̃ɡʃ.

Ƀɘ Ůĵɤ ɛŰŰɒɣɡʃ əŬɔ ɡĵɤ ůŰ̃ɒɣɡʃ ɛgůdŮɡʃ Ű̃ɛg ɛůɒɘɕi ŭŮɜ Ůdĵ ŮƳɡŮɜgɜ Ű̃l ŭgůɘɕɘɔɛɘɐ ɘŮŰ̃ɛgĵɔɑŬ Ű̃ɛg Ŭɔɑĵı´ɘɛg ɡĵɔŬɔɘůɛɑi, Ŭ ɛŰ̃ɒɕiɜ ɦɛɤɡʃ əŬɑɡĵɘɛůŰ̃ɒɕiɡʃ´Ůĵ ƔɔɜŰŰɡʃ Ůɘɛɔɛɑɡʃ Ŭ ɦ Ű̃ɛɜ əŰŰŰɔŬɔɤ Ű̃ɐ (Ūĵ Ůůgɒɕiɘɛg et al. 2002).

1.1.3 Biologické účinky medu:

Již od starověku je med používán, jak jako potravina, tak i jako lék. Jeho léčivé účinky jsou dány jeho složením, kdy obsahuje velké množství cukrů, vitamínů, minerálních látek, enzymů, aminokyselin a dalších látek, které mají antibakteriální, antioxidační, protizánětlivé a imunostimulační účinky (Bogdanov et al. 2002).

V současné době se med používá jako součást léčby různých onemocnění. Nejčastěji se jedná o onemocnění dýchacích cest, kdy se med používá jako součást léčby kašle, chrapotu a bolestí v krku. Jeho účinky jsou dány jeho složením, kdy obsahuje velké množství cukrů, vitamínů, minerálních látek, enzymů, aminokyselin a dalších látek, které mají antibakteriální, antioxidační, protizánětlivé a imunostimulační účinky. Obecně, med snižuje množství bakterií v dýchacích cestách a tím zmírňuje příznaky onemocnění. Nejčastěji se jedná o bakterie rodu Streptococcus, Staphylococcus a Haemophilus. Nejvíce se používá med manuka, který má nejvyšší antibakteriální účinky. Jeho účinky jsou dány přítomností methylglyoxalu, který je obsažen v nektaru z květů manuky. Jeho množství se pohybuje od 100 do 500 mg/kg, v závislosti na kvalitě medu (Alvarez-Suarez et al. 2010).

1.1.4 Δασικές εκτάσεις :

Η επαναγγίσεις δασικών εκτάσεων, που ορίζονται στο άρθρο 3 παρ. 1 του Ν. 998/1979 (Carnwath et al. 2014). Σε αυτές περιλαμβάνονται και εκτάσεις που χαρακτηρίζονται ως δασικές σύμφωνα με ειδικές διατάξεις της δασικής νομοθεσίας, οι οποίες δεν έχουν ακόμη κηρυχθεί οριστικά δασικές. Σε αυτές τις εκτάσεις δεν επιτρέπεται η εγκατάσταση νέων δραστηριοτήτων εκτός από εκείνες που προβλέπονται ρητά από τις διατάξεις της δασικής νομοθεσίας.

Στις δασικές εκτάσεις περιλαμβάνονται και οι εκτάσεις που έχουν καταστραφεί από πυρκαγιά και οι οποίες χαρακτηρίζονται ως καμένες δασικές εκτάσεις. Στις εκτάσεις αυτές απαγορεύεται η εγκατάσταση νέων δραστηριοτήτων για δέκα χρόνια από την πυρκαγιά.

<u>i) Σε υψόμετρο:</u>

Το 65% των δασικών εκτάσεων στην Ελλάδα βρίσκεται σε υψόμετρο. Το μεγαλύτερο μέρος αυτών των εκτάσεων καλύπτεται από δάση της *Marchalina hellenica* και από «δάση» που χαρακτηρίζονται ως καμένες δασικές εκτάσεις. Το μεγαλύτερο μέρος των δασικών εκτάσεων στην Ελλάδα βρίσκεται σε υψόμετρο μεταξύ 500 και 1.000 μέτρων. Το μεγαλύτερο μέρος των δασικών εκτάσεων στην Ελλάδα βρίσκεται σε υψόμετρο μεταξύ 1.000 και 1.500 μέτρων. Το μεγαλύτερο μέρος των δασικών εκτάσεων στην Ελλάδα βρίσκεται σε υψόμετρο μεταξύ 1.500 και 2.000 μέτρων. Το μεγαλύτερο μέρος των δασικών εκτάσεων στην Ελλάδα βρίσκεται σε υψόμετρο μεταξύ 2.000 και 2.500 μέτρων.

<u>ii) Σε κλίση:</u>

Η πλειοψηφία των δασικών εκτάσεων στην Ελλάδα βρίσκεται σε κλίση μεταξύ 5-10% και μεταξύ 10-20% στην περιοχή της **Ελάτης της Κεφαλονιάς** (*Abies cephalonica*) και στην περιοχή της **Ελάτης της Ευβοίας** (*Abies alba* και *A. pectinata*) και στην περιοχή της Βόρειας Πίνδου (βορειοδυτική Ελλάδα). Το μεγαλύτερο μέρος των δασικών εκτάσεων στην Ελλάδα βρίσκεται σε κλίση μεταξύ 10-20% και στην περιοχή της Βόρειας Πίνδου. Το μεγαλύτερο μέρος των δασικών εκτάσεων στην Ελλάδα βρίσκεται σε κλίση μεταξύ 20-30% και στην περιοχή της Βόρειας Πίνδου.

[illegible]:

[illegible] (*Castanea sativa*), [illegible] *Myzocallis castanicola*. [illegible] Caillas, (1971), [illegible].

[illegible]

[illegible] 10% [illegible] «[illegible]» [illegible].

[illegible]

[illegible] «[illegible]» (*Erica verticillata*), [illegible] (*Erica arborea*), [illegible] (*Arbutus unedo*) [illegible] (*Rhododendron*). [illegible].

[illegible].

¢ε εγəɔ əεgεŰɻɘŸƒ ŮʁŰɔ Ű£ɜɤ Ű§ɔɦ ɔɘŰ ŰŰ εŮɔɑůɯɘŰ, ɦεɤƒ g´ɦ´ɘɻε ɔɘŰ Ű£ɜ Ÿɜɑɻɤ´ε əŰɔ εŮ´Ůɻɘɻɯ£εγɜɑ Ů£´εɻəɔε ŰɔɑŰ. ¢εγəεgƒ, Ű£ εγəɔ Λεŭɦ̃ŭŰɔŭɻεg ´ɻɘɜ ɤɻɘŒŸůŮɔ´Ůɻɘɣ̃gŮɔ Ű£ɜ εgůɑŰŰɔŭɻεεŮűε£Ű£ɜɔɑɑ, ɑε´εɑŰŮʁŰɔŰ£ɜɔəɔε Ű§ůε ɔɘŰ Ű§ƒ εγəɔ̊ůůŮƒ, ɦůε əŰɔ ɔɘŰ Ű£ɜ Ÿɜɑɻɤ´ε. ȳŰŰɜ Ű£ εγəɔ ɤɻɘŒŸůŮɔ ´əɔɻɤgƒ ɑ Ű£ɜɔəɦŰ£ŰŰ Ű£ɑƒ εgůɑŰƒ ŰgŰ£gƒ ŮɔŰűŰɔœŮŰŰɔ

<u>Ɛ̈Ű)ɀ γəɔ¢ əɑŰɔɑεg:</u>

Ƀ ¢ əɑŰɔɑεgƒ ůŰ£ɜ ɑɩ ɻŰε ŰgƒŭœŮɔ ε Ůɔ Ÿɔɑ´ŰɻŰɔɤɔε ε Ůɔɔɔɛi ´εg ŮœŰɔ ´əɛi ůɔɛ ůŮ´ɛəgűŰɔɦɔŮƒ εɔ ε´ɛɑůƒ ´Ű£ɛgɜ ůɑεŰɔŰ£ɔɦɻɔŮƒ ŰɔɔŰűɻɛűεgƒ. ÕεGŮɔɓɛgŰ£ɻɤ ŭɑɻɔŮ¡ůɑ.

<u>Ć) ¢ε εγəɔɓŰεɓŰɔɔɛi:</u>

ÁœŮɔ ε ɑŰŮ ɦ Ű§ƒŰɛɔŮ§ƒəŰŰ£ɔɛɻɑůƒ ε Ůɔɔɔɛi ´εg ´Ůɻ ŸɔŮɔ ɑ ÁəɔŸűŰůŮε Ůɔ Ÿɔ Ůƒ´ε ů ɦŰ£Ű§ƒ. ¢ŮŰŮɔ Ůg Ű£ŮŮŰɔŰɔɻɦɜɔŰɑ ´Ůɻ Ůɔɤɔε Ű£g ´ŮɻɔɛɻɑůŰ£əŮ ůɑεŰɔŰ§ɔŸ əɦɔɤ Ű§ɤ ε Ůɔ Ÿɔɔɤɜ Ů ɤəŮɜ ´εg ´ɻɔəŰɔɛi ɜŰŰɔůŰ§ƒ ε γəɔůůŮ§ƒ Ů ŰŰ ű gŰ£ű Ÿɻ ε Ůɔŭ, əŰɑι g Ů ɑůɑƒ əŰɔ Ů ɦ Ű§ƒ ε əɔɻγ g Ů ε ŭɦ ůŮ§ƒ ɜγəŰŰɻεg Ű§ɤ ɜγɤɤ ɜ əŰɔəɔŮɻɔɛi ε Ůɔɤɜ Ű gŰ£ɔɦɜɔε ɤɜ ´ε əɔəɔɑɜ ɓŰεɓŰɔɔɛi. Ƀə ε γəɔůůŮƒ ůgəəɔγɔεgɜ ɜγəŰŰɻ Ů ɦ Ű ɔɑɔŸəŰɔůɔɤ Ű ɔɑɔŸɜůɔŰŷɻɔŭ Ű£g ű gŰ£ɛi, əŰɑι g Ů ɑůɑƒ əŰɔ Ů ɦ ε Ůɔɑű ε Ů ´εg Ůɔəɻɔ Ű Ů ɦ ŭɔŸŰε ɻŰ ε Ů ŰŰ ε´ɛɑŭ ´Ůɻ Ůůɔɑű£ɛi ɜ Ű£ɜ əŰɔəɔγɻɔůŭ. ɻ ɜŰɑŰŰ ε Ů Ű£ Ű§´ɔɦ ůəεŰŰɔɦɑɻɤ ε ε γəɔ ε Ůɔɔű ε Ÿű ɜ, Ű£ ε γəɔ ɓŰεɓŰɔɔɛi Ů ɦ ε Ůɔɑű ε Ů, ŮœŰɔŰɔɔɛɜŰɦɑɻɤ ε ε əŰɔ ε Ů ɔɔγƒ ű ɻγƒ ŭŮɔ γɑŮɔəŰɔɔ ɔŮůɑ.
¢ε ɓŰεɓŰɔɦ ε Ůɔɔ ´εg ´ɻ ε γɻɑŰŰɔ Ů ɦ Ű£ Ÿɔɑ ƒ, ŮœŰɔ Ů ɑůɑƒ ŮɔɔɛɜŰɦɑɻɤ ε ε Ů ɑŰɻŰɔŰɔɻɦɔŮɔɛ ɓɑŰɻɤɔε ɔŮůɑ.

<u>¢) ɀ γəɔŮů´ŮɻɔŭɑŮŭɩ ɜ:</u>

ÁœŮɔ Ůɻɤ ε ŰŰɔɦ ε Ů ɔŭɔŰŰŰɻŰ əŰɔŸ ɑɻɔŰɔəɑ´Ű£ɔŸ ɑŰɻŰŰɔɦ ε Ů ɑŰɻŰɔŰɔɻɦɔŮɔɛ ɓɑŰɻɤɔε ɔŮůɑ.

Ʉɑɔ: ŪɻŰůgɓɑi əɑg et al. 2002

1.1.5 Bűyəd ůŰłɜ gɔŮŰ:

¢ɛ ɛyəɵ ´ɟɛůűɣɟŮɵ ´əŮɛɜŮəŰɛƐŮŰŰ ɦůɛ ŰűɛɟƳŰɛɜ yəŮɔɛ ŰłɡŮ ŰɜƳŮɣɜdɡ´ɛəəɪɜ ɛɵɟɛɛɟɔŰɜəůɛɪɜ ´ɛg ůɛŮŰɶɛɜŰŰɔ ɛŮ ŰůdyɜŮɵŮɡ ɐ ɛɛəɨɜůŮɡ əŰɔ Ułɜ dŮɟŰ ŮŰŰ ɛɟəůɛyɜɤɜ ´ɟɛɓədɛƳŰɤɜ gɔŮŰŰɡ. Á´ɕ´əyɛɜ ŮɛűŰɜɶŮɔ´ɛəɵəŮɡ ɓəəɔɛɔəyɡŮ ŰəűɟƳůŮɡ əƳɛəŮɡ ŰŰɦ Ůɡ ɛ´ɛdŮɡ ŮɵŰɔ d ŰɜŰɶəɵɟɛɓəŰɔɐ, d ŭɟƳůd Ułɛg ɤɡ ŰɜŰɶɛɜŮəűɤŰəɦ, ŰɜŰəɦ əŰɔ ŰɜŰ´ŰɟŰůəŰɔɦ. ò əəŮɡ ůdɛŰɜŰəyɡ Ułɛg ŭɟŰůŰłɟɦŰłŰŰɡ ŮɵŰɔ d ŰɜŰűɪəŮɔɛɜɪ ŭdɡ, d ŰɜŰɶŮŰɔəŰəɔɦɜɛɡƒəŰɔ d ŰɜŰəŰɟɶəɵɐ. ¢ ŮəəɛədŰɛɟɐɔdůdɡƒ ɔəŰ Ułł dŮɟŰ ŮɵŰ Ű´ɜ Ű̃ɟŰgɛƳŰ´ɜ, d yəəŮəɣd ´ŰɟŮɜŮɟɔŮɜ ɜ ůŰłɜ ŰɜŰɔɛɨűəůd Ułɛg ɔŰůŰɟəɛɨ ´ɦɜɛg əŰɔd ůgɜŰɦɛŮəůd ŰłɡƒŭəƳɟəŮŰłɡƒŭəƳɟɟəŰɡŰ ɛŰŮɔɛɨɜ ´ɟɦůdŰŰŰ dŰŰəƳɛGŰɟŰɔŰłɟəůŰəƳŰɛg (Alvarez-Suarez et al. 2010).

ɟ) ɟ ɜŰɓbŰɔŰłɟəŰɔɐ ŭɟƳůd

Bɵ´ŰɟƳɔɛɜŰŰƒ´ɛg ŮəgdɨɜɛɜŰŰɔ ɔəŰ Ułɜ ŰɜŰɓbŰɔŰłɟəŰɔɐ ŭɟƳůd Ułɛg ɛŮɔəɛɨ ŮɵŰɔ d gɣdəɐ ɤůɛɤŰəɦŰłŰŰ, d ɛɜɨŰłŰŰəŰɔ əŭəŰŰŰɟŰŰɛ g´ŰɟɛɜŮɵŭɛ Ułɛg gŭɟɛɔɦɜɛg, ´ɛg ůɑdɛŰŰɑŰŰɔŰ ɦ Ułɜ ɛɜŮɵŭɤůd Ułłgƒɔəgəɦɛdłgƒ ŰŰ ɦ Ułɛ yɜɛgɛɛ ɛɜŮəŭƳůd Ułłgƒɔəgəɦɛdłgƒ, ´ɛg ´ɟɛyɟɑɛŮŰŰɔŰ ɦ Ułɛggƒg´ɛűŰɟgɔɔəɛɨgƒŰŭyɜŮƒŰɤɜ ɛŮəəůůɪ ɜ, əŰŰƳŰłůəƳɟəŮŰłɡƒ ´Űɟəɦŭɛg ɤɟɑŒŰəůdɡƒ. ȳŰŰɔ Ułɛ g´ŰɟɛɜŮɵŭɛ Ułɛg gŭɟɛɔɦɜɛg ŭəŰů´ƳŰŰɔ ɛŰ´ɟɛůdɐəd əŰŰŰəƳůdɡƒ, ɛŰɟəəƳ ɛyəəŰ ůgɜŰɛɑɛgɜ ɜŰ´ŰɟɛgůəƳɛgɜ ůdɛŰɜŰəɐ ŰɜŰɓbŰɔŰłɟəŰɔɐ ŭɟƳůd ´ɛg ŰɜŰűɣɟŰŰɔɤɡƒɛd-g´ŰɟɛɜŮɵŭəŰɔɐ ŰɜŰɓbŰɔŰłɟəŰɔɐ ŭɟƳůd. ¢ɣŰɛəɛg ŮɵŭɛggƒŰɟƳɔɛɜŰŰƒŮɵəŰɔd əgůɛɛɨɛd, ŰŰűŰəɛəəəƳɛɜɣŰəŰɔŰŰűəŰɔɛɜŮəŭɛ. UɟɛŰŰɵŰŰɔɦůŰɛ əɨɟəɛ ɛyɟɛɡƒ Ułłgƒ ŭɟŰůŰəɦŰłŰŰƒ ŰgŰɛɡƒ ɛ´ɛɟŮɵɜŰ yɑŮəɵŰłɜ ůgɜŰłɟdŰəɐ ŰɨɜŰɛdłɛg ɛŮəəɛɨ, Ułɛ ɛ´ɛœ ɛŮəɨɜŮəɔ Ułɜ Ůəɛgɛəəɐ ŰɛŰɨɟɤůd Ű̃ɤɜ űɟɛɨŰɤɜ əŰɔ ´ɟɛəŰɛɓƳɔůəŰłɜ əə´əŭəŰɔɐ ɛɜŮəŭƳůdɡƒ (Mundo et al,2004).

ɗb) ɟ ɜŰɶəɜŮəŭƳŰəyɡƒəŭəɦŰłŰŰƒ

ɟ ɜŰűɣɟɛɜŰŰɔ ůŰłɜ ŭgɜŰŰɦŰłŰŰ Ułɛg ɛŮəəɛɨ ɜŰ ɛŮɨ ɜŮəɔ Ułƒ ɛɜŮəŭƳŰəyɡ ŰɜŰəŭɟƳůdɡƒ, ´ɛg ɛ´ɛɟŮɵɜŰ´ɟɛəŰɔyůɛgɜ ŭdəɑŰłɟɡɨ ŭŮəƒŰɜŰəŭɟƳůdɡƒ ůŰŰ Ű̃ɟɦűɛŰəŰɔ ŭgůɛŮɨŮəƒ ŰƒŮ ůŮəƒůŰłɜ gɔŮŰŰ, ɦ´ɤɡɛɟɦəŮƒŰůdyɜŮŮƒəŰɔəŰɟəɑɛggƒ. ¢ŰŰɜŰəŭɶɜŮəŭƳŰəyɡ Ułɛg ůɶűŰɜɶŮɔ´ɛəɵůgɛɓƳɔůɛgɜ ůŰłɜ ŰɜŰəŭɶɜŮəŭƳŰəyɡ Ułɛg əŰɔɦŰłŰŰ.

Bɵ űŰɜɛəɵyɡ Ůɨ ůŮəƒ ůgɛɓƳɔəɛgɜ ůdɛŰɜŰəƳůŰłɜ ŰɜŰəŭɶɜŮəŭƳŰəyɡ əŰɔɦŰłŰŰ Ułɛg ɛŮəəɛɨ, Ű̃əƳŭŰɨ ŮɵŰɔ d ŰɜŰəŭɶɜŮəŭƳŰəyɡ´ŰɟdgɜŮƒɔəŰŰgŰɛ. Á3ŰɛɨŰɛəgƒ, d ŰɜŰəŭɶɜŮəŭƳŰəyɡ əŰɔɦŰłŰŰ´ɛəɑəəŮɨůŰɛŮɔƳɛɔ ɓŰdɛɦ ŰɜƳəɔŰɛŰłɜ ´dɔyɐ Ű̃ɤɜ Ƴ3dŰɤɜ Ułɛg ɛŮəəɛɨ, ´ɑdŰɨɜ əɦɔɤ Ű̃ɤɜ ŭəŰűɛɟɤɨɜ ůŰɛ ´ŰɟəŮɛɦɛŮɨɛ űgŰəɨɜ ŭŮƒŰűɟɛɔŮɨɜ ɛŮŰŰɓəəŮɨɜ əŰɔŮɨɑɛgɛəəɐgƒŭɟŰůŰłɟəŰɔɦŰłŰŰƒ.

Ʉɋ ŰɔɛɘɛɔŰŰŰɔ´ɤɠűŰűɛɣɜɛɠ ɧŰɔɖ ɛɣůɖ ɔɘgəŰɜŰɔɘɐ ´ɻɧůəɖɣɖ ŰɻɧŰɛɜ Ɣɜɖɻɤ´ɛ ŰɔŰɛƔŰŰɔ ɧŰɔ ŰɯŰɔ ´Ɣɜɤ ŰɻɧŰɛɜ ŰɻɧŰɛɜ 70 kg/ɣŰɛɠ, ɖ ɠ´ɛəŰŰƔůŰŰůɖ Űɻɤɜ ´ŰɻŰűɛůəŰɔɪɜ ɔɘgəŰɜŰɔɘɪɜ ɛgůəɤ ɜ ŰɻɧŰɛ ɛɣɔɘůŰɛɻəůɛɣɜŰŰɻɧűɛŰɖŰɛ´ɛɻɛɨůŰɜŰɛŭɖɔɐůŰɔůŰ Űɔəůɛgɛɣɜɛ ŰɜŰɔɛɜŰɔɘɔɻɤŰɔɘɧ ůɨůŰɖɛŰƔɛgɜŰŰɻůŰgɔəŰɖŰɻɛɐɔɘŰɠ.

ű) ɻ ɜŰɔɛŰŰŰɔɘŰɜɔɘɧɜɛɠɖ, ŰɜŰɔɘŰɻəɜɔəɐ əŰɔŰɜŰűíɔəŰɔɛɛɜɪ ŭɖɠɖűɻƔůɖ

Ō ɛŰɔ ŰɻɛŭŰɔɛɖŰɔɧŰɔ ŰɔɛɣɔɔɛŰɔɪ ɜŰɔ Űɖɻ ű ɔəŰɔɛɛɜɐ ŰɔɛgɻɣɣɛŰŰɔɛɠ, ŰɔɛɛɑŭɖɛŰ əŰɔ ŰɖɻɜɔŰɻɤůɖ, ´ɻɛƔɔŰɔ Űɖɻɜ Űůɛɨɔɤůɖ ŰɔɛgɻŰɻɛŰŰɔɛɠ, ɛŰɔɪ ɜŰɔ ŰɔɛɛɣɔŰŰɛɠɖ Űɖɻɠɛgɔɤɛɠ əŰɔ ŭɤŰɔŰɻɠ ŰɔɜŰɔɣɜɜɖůɖ Űɻɤɜ ɤůŰɪ ɜ. Á´ɵ ɔɤɣɛɜ ´ŰɻɻŰɛŰŰɔƔűŰɜŰŰɔɧŰɔ´ŰɻɛgůɔƔɛŰɔ ŰɜŰɔŰɔɔɛɔŰɜŰůŰɔɐ ŭɻƔůɖ ůŰ ɧɔəɛgɠɠ əŰɔ ŰŰ ŰɜŰɔɛɜɔŰɔɤŰɔƔ ɛ´ɛɻŰůɪ ɜŰ ŰɠŰɻɣɣɛgɜ Űɖɻɜ ŰɔƔ ɔɤůɖ Űɻɤɜ ɛŰŰŰůŰŰɔɪ ɜ əgŰŰƔɻɤɜ. ɛɵ ŭɻƔůŰɔɠ ŰɛgŰɻɣɠ űŰɜŰŰɔ ɜŰ ɛűŰɔɔɛɜŰŰɔ ůŰɛɵŰɔɔɛɜŰŰɔ ůŰ ɛɵŰ ůŰɔɠƔ ŰɠŰɻɧ ɛɖɛɔɤɣɠ ɛgůɖŰɠ ´ɛg ´ŰɻɛɣɛŰɔ əŰɔ ŰɔɜŰɔ ´ɻɛɔɤůɛɣɜŰɠ ɛŰ ŰɜŰɔɛɜɔŰɔɤŰɔƔ Űɖɻɜ/ŰɜŰɔɛűíɔəŰɔɛɛɜɪ ŭɖ ŭɻƔůɖ. ¢ɣŰɛɵŰɠ ŰɔɜŰɔ űŰɜɛɔɤɔƔ ´ŰɻƔɔɤɜŰɛɻɜɜɔŰűŰɔɐ ůŰůgɜŭgŰůɛɧ ɛŰƔɔəŰɠɛgůɖŰɠ.

ɋ) ũŰůŰɻŰɜŰŰɻɛɔɛɔɖŰ

Ƀɵ ɔɛɛɪ ɜŰɠɠŰɛg ŰɜŰŰɻɤɔɛɨ ůɤɔɐɜŰŰɔɜŰɔ ůgɛɜɣɠůŰɧɔɛ Űɛɜəɧůɛɛ əŰɔŰɖɻŰƔɛgɜ Űɜɖɻɪ ´ɛggɠɧɔɤɜ Űɤɜɖɔɔɤɜ. ¢ɛ ŰɔɜɧɛɣɔɵɣɠŰůɔɓŰɔŰŰɻɤɜɔəŰŰɧɜɛ ŭɻƔůɖɻɣɜŰɜŰɔ´ɛɔɔɪ ɜ ŰɜŰŰɻɛ´Űɖɛɔɧɜɤɜ ɛɻɔŰɜůɛɪ ɜ. Á´ůɖɠŰ ɛŰŰɔůɔɤůɛgɻɧ ŰɜŰůŰɛɔɣŰŰɛg *Helicobacter pylori*, ´ɛg ´ɻɛəŰɔůɪ´ŰŰɔƔɣɔəɖ əŰɔɔŰůŰɻɖŰɠŰůŰ ¢ɣɔɛgɠ, ɓɻɣɠɖəŰɜŰůgɜŰɛɛŰɜŰŰɖ ŭƔɻəŰŰɖŰŰɖŰŭƔɻɛɔŰŰɻɤŰɔɐ ɔŰůŰɻŰɜŰŰɻɖŰ.

ò ɔɘɔŰɠ ůɖɛŰɜŰɔɘɣɠŰŰɻƔůŰɠŰŰɛg ɛŰɔɔɛɨ ůŰɖɜ Űɜɖɻɪ ´ɔɘɖ ´ɣɣɖ ɣɛɛgɜ ůgɜŭŰɖŰůɪɛŰ ɛɔɔɛůŰɔɛŰɻɖŰɠ. ɻ gŰƔ ŰŰ ůgůŰŰɘɔƔ ŰɛgɛŰɔɔɛɨ ɣɛɛgɜ ´ɻɛɓɔɛŰɘɔɐ ŭɻƔůɖ, əŰɖɪ ɠ ŰɠɜƔɜɛgɜ ŰŰBifidobacteria əŰɔŰɛggɠɔŰɔŰɔŰɛɓƔɔɵɔɔɛggɠ.

Á) 7ŰɻŭɵŰɔůɔŰɔɣɠŰůɣŭɻƔůŰɠɠ

ɻ ´ɧ ŰɛŰŰɔɣůɛŰŰŰ ɣɻůgɜŰɠ űƔɜɖəůɧɧŰɻɖ əŰŰŰɜƔɔɣůɖ ɛŰɔɔɛɨ ɛŰɔɪ ɜŰɔ Űɛggɠ əŰɻŭɵŰɔůɔŰɔɛɨ ɠ´ŰɻƔɔɛɜŰŰɻɠ əɜŭɨɜɛg, əŭɜŰŰŰɻŰůŰɛŰŰɠɜɖəɣɜɛg əɜŭɨɜɛg. ɋŰɔ ŰɠɜƔɜůɔŰɛɻůɛ ůɤɛŰŰɔɧɧ ɓƔɻɛgɠ ůŰɻɛŰŰɔɧ ɓƔɻɛgɠɧůɔɛ əŰɔŰɛg ůɤɛŰŰɔɛɨ əɑɛggɠ. ¢ɣɔɛgɠůŰɜŰɔɛɨ ɠŰůɖŰɔŰɔŰɻɠ ŰɛɔɖəɧŰŰɻɖ Űɨɜɖůɖ ŰŰɻɠ ɔəgəɧɛɖɻɠ ŰɛgɛɻəɧɖŰɻɖ ŰŰɻɠ ´əƔůɛŰŰɛgŰɧɧɧŰɻɖ ŭŰɜŰɻɧɛɖ. (Alvarez-Suarez et al. 2010)

1.1.6 [illegible]:

[illegible] Gram [illegible] Gram [illegible] 80 [illegible] (Vica et al. 2014).

[illegible].

[illegible]

[illegible] (O_2 + [illegible] + H_2O_2). [illegible] H_2O_2 [illegible] (Ewnetu et al. 2013).
[illegible] H_2O_2 [illegible] DNA- [illegible] H_2O_2 [illegible] H_2O_2 [illegible] H_2O_2 [illegible] (Alvarez-Suarez et al. 2010).
[illegible]

[illegible] (MGO)

[illegible] (MGO) [illegible] Manuka. [illegible] MGO [illegible] MGO [illegible] Manuka [illegible] (DHA) [illegible] *L. scoparium*. [illegible] DHA [illegible]

ɜɣəÚÚɻ əŬə ɔɵŬÚn ŮɷŬə ´Ŭɻɕi ůŬ ůŮ Úɦůɕ ɛŮəŸəŬ ´ɕůŸ ůÚŝ ɜɣəÚÚɻ Úŕɜ ŭɣɜÚɻɤɜ Manuka. ¢ MGO ŮɷŬə Ů ɑůdɠ´Ŭɻɕi ůŬ ůŮɛɵɻɦÚÚɻŮɠ´ɕůɦÚɺÚÚɠəŬə ůŮɛɣəɵŬ Ŭŕɦ Ÿəə Ŭű gÚŝəŸŮɷűd.

ũ) Bee-defensin-1

¢ɕ ɛɣəɵ´ŮɻɵɣɢŮə ɣɜŬ ŬəŬŝɛɵɻɕɓɵŬəɦ´ŮÚɷũɷ, Úɺɜ bee-defensin-1 ´ɕg ůgɛɓŸəəŮə ɕgůɵŬůŬŝəŸ ůÚɺɜ ɓŬəÚɺɷəəÚɦɜɕ ŭɻŸůd ɣɜŬəŬə Gram dŮÚŝəı ɜ ɓŬəÚɺɷɑɷɤɜ ´.ɢ *S. aureus*. ¢ bee-defensin-1 ŮɷŮ´ɻɕdɔɕgɛɣɜɤƒ ŬŕɕɛɜɤdŮɷŬɦ Ŭŝɜ ɓŬůɵəɵəɦ´ɕəÚɦ (ɔɜɤůÚ ɤƒ royalisin), Úɺɜ əi ɻɵŬ´dɔə ŰɻɕűəƒɔɵŬ ÚɺƒɓŬůɵəɵɣƒ´ɻɕɜi ɛűŮƒ, əŬə ŬəŬɔɜɤɻɑůÚɺəŮůÚɺɜ Ŭəɛɕɣɛűɕ Úŕɜ ɛŮəɵůı ɜ. Ƀ ɓŬůɵəɵɦƒ´ɕəÚɦƒ´ŮɻŸɔŮÚŬə ŬŕɦɜɣŮƒ ŰɻɔŸŰɻɵŮŮƒɣɵəɵůůƒəŬə´ŮɻɵɣɢŮə ŬɵəŸůůƒ ɛɣəɵůůƒəŬə´ŮɻɵɣɢŮə ŬɵəɻɑůdŰŕɜ ŬűɣɜɤŬŝɠ ɕg ɠűŸɻgɔɔŬ ɕ mRNA Úɺƒ bee-defensin-1 ÚŬgŬŝ´ɕəɾdɺəŮůŬŝɜ ɠ´ɕűŰɻgɔɔəɦ ŬűɣɜŬ Ŭŕɜ ɜŮŰɻı ɜ Ůɻɔ ŬŰɻɤı ɜ ɛŮəɵůı ɜ, ɠ´ɕŭɺdɵı ɜɕɜÚŬƒɦŮə ŬgŮɦƒɠɕ ŬűɣɜŬƒŮɷŬə´ɕg Ůɛ´əɣəŮÚŬə ůÚɺɜ ´ŰɻŬɔɤɔɐ əŬə i´Ůɻɵɣɐ Úɺƒ ůŬŝɜ ɓŬůɵəɵɦ ´ɕəÚɦ. ȳÚŬə ɕɵ ŮɻɔŸŰɻɵŮƒ ɛɣəɵůůƒ ɛŮəŬəı ɜɕgɜ, ɔɷɕɜÚŬə ɕɵ ɛŮəŬəi ŰɻɕɜɕɵŮɻ´ŰɻŬɔɤɔɑ ɛŮəɵŝi. ζ ɵɻɣƒ ŭɵŮűɕɻɣƒ ŮɛűŬəɷɕɜÚŬə ɛɕɻűɕəɕɔəŸ ŬəəŸ əŬə ůŮ ŮɗůŬɕ ´ɻɤÚŮɷɵəƒ ɣəűɻŬůdƒ Ŭŕɜ ɠ´ɕűŰɻgɔɔəı ɜ Ŭűɣɜɤɜ Ŭŝgƒ. Ƀɵ ɛɣəɵůůƒ´ɻɕůdɣŬŝgɜ Úɺɜ ɣəəɻɵůd ŰɻɦŬŝgƒ ɠ´ɕűŰɻgɔɔəɕi ƒ ŬűɣɜŬƒŮɷŬŝgƒ ůŬŝ ůgəəŮəɛɣɜɕ ɜɣəÚÚɻ. ¢ i´Ůɻɜd Úɺƒ bee-defensin-1 ůŬŝ ɛɣəɵ ɠ´ɕŭdɔı ɜŮə ɦŮə ɛŮŰŸ Úɺ ɛŮŰŸɓŬůd Úɺƒ əŮəŬŝgɻɔdŰƒ Ŭŕɜ ɠ´ɕűŰɻgɔɔəı ɜ Ŭűɣɜɤɜ Ŭŕɜ ŮɻɔŸŰɻɵŮƒɣɵəɵůı ɜ ɛŮəɵůı ɜ ɛŮÚɺɜ dəɵəɑŰ, ɕ ŬűɣɜŬƒŮɷŬəɕəɕgɑŮəɜŰÚɺɜ´ŰɻŸɔŮəɻ gÚɦ Ŭŝ ´ŮÚɷũɷ, Ů ɕɛɣɜɤƒ, ´ɑŰɔɦɜ ůgɛɓŸəəŮə ůÚɺɜ ´ɻɕůÚŰůɑŰ Ŭŝgɓŭəɵɕi ´ɕəÚŝi ŬəəŸəŬəŬŝg ɛŮəɵŝi ɣɜŬəŬəɕɛɵɻɕɓɵŬəɑƒŮəɕɤ ůdƒ (Kwakman et al. July 2010).

¢ ´ŮɻɕgůɑŰ Úɺƒ bee-defensin-1 ůŮ ŭəŸűɕɻŰ ɛɣəɵŰ ŭŮɜ ɣƒŮə ŮɻůɜɑdŮəůgůÚɺɛŰÚəŸ ŬəɦɛdəŬə´ɕůɕÚəŸ ŭŮűɕɛɣɜŰůƒÚəŸɛŮÚɺ ůgɔəɣɜŰɻɤůd ŬgÚŝi Ŭŝg´ŮŬŭɷɕg ůŬŝ ɛɣəɵŭŮɜ ɣƒɕgɜ ŬəɦɛŰŰəɛdɻɵɤdŮə

ɷ) ŸŬɻɕgůɑŰŮó ɻɦůdŮÚɤɜ ůgůŰŰÚəı ɜ

Ásɷŭəŭi ůəɕəɕ ɜŰəŰdɕɻɵůŮůŮ´ɕɵɕ ɓŰdɛɦ d MGO əŬəd bee-defensin-1 ɐ ŬəɦɛdəŬə ɛd ŰŰgŬŝ´ɕɵdɛɣɜŰ ůgůŰŰÚəŸɛ´ɕɻi ɜŰ ůgɛɓŸəɕgɜ ůÚɺ ŭɻŬůÚəɦƒÚɺŰŰŬŝg ɛŮəɵŝi. Ɉ´Ÿɻɕgɜ ´ŮɻɦəŰ ŬgŮŸɛŮɵɣƒ ŮəŭŮəɷŮƒɔɵŰÚɺɜ ŮəŭŮɑŮƒɔɵŰ ÚɺɜŮəŰɜ ´ɕg ůgɛɓŸəɕgɜ ůÚɺɜ ŬəŮɓŮəŬÚɺɻɵŮəɐ Ŭŝg ŭɻŸůd, əŰı ƒɛŮŸŰ ɦ ŮəɕgŭŮŰɻɣɤůd Ŭŝg H_2O_2 əŬə Űɛűɦɛdůd Ŭŕɜ ´ɻɤÚŮɷɵəı ɜ Ůəı ůŰɜ, ´ɕəəŸɛɣəɵŰ ŭɵŮÚɺɻɕi ɜ ÚɺůŰɜ ´ɕg ůgɛɓŸəɕgɜ ůÚɺɜ ŬəɦɛŰŰəɛdɻɵɤdŮə ŮəŭŮəɷŮƒɔɵŰÚɺɜ əŸ ɕɤɜ ɛɵɻɣɕdŮəɛɵɻɕɓɵŬəɑƒı ɜ.

¢ ÜɜÜÆɛəɲɹɛɓɘÜəɐ ŭɲŸůɖ Üɛg ɛÜəəɛi úŬɜÜÜÜɜŬ ɛűÜəəÜÜÜɜ ůÜɬɜ ɛɜi ÜɬɬÜŬ əÜɜ ÜɬɜɤůɛɤÜəɦÜɬɬÜŬ Üɛg. Á´ɘ´əɐyɛɜ ůgůÜÜÜÆəŸ Üɛg ɛÜəəɛi, ɦ´ɤɠ ŬɲɤɛŬÜÆəŸ ɛɜɐyŬ ɐ űŬɜɛəəɐyɠÜɜı ůÜÆɠəÜɜŸəəůɠɛɖ ɢÜɲÜɜÜɬɲɐůɛɣɜÜɠɛgůɖůɠɛ´ɛɲÜůɜŬůgɛɓŸəəɛgɜ ůÜɬɬ ůgɜɛəɐəɐ ÜɜÜÆɛəɲɹɛɓɘÜəɐ ŭɲŬůÜɬɲɐɦÜɬɬÜŬŸ Üɛg. ȳůɛ ŬÜíɛɲŸ Üɬɜ ɤůɛɤÜəɦÜɬɬÜŬ, ůɨɔəɲɐůɖ Üɛg ɛÜəəɛi ɛŮŭɐŸəgɛŬ¢ŸɢŬɲɖɠɠŭÜɢɜÜəɦÜɐÜgÜŬɐ əÜɔɛɦɜɛ ŭÜɜ Üɜɖɔ·Üů´əɐɲɤɠ ÜɬɬɜÜɜÜÆɛəɲɹɛɓɘÜəɐ ŭɲŸůɖ Üɛg ɛÜəəɛi əŬůı ɠÜɛ ŭɐŸəgɛŬ¢ŸɢŬɲɖɠɠŭÜɜ ÜɜŬůÜɲəəÜəÜɬɬɜ ÜɜŸ Ûɠɜɖ Ûɤɜ ɓÜəÜɬɲɑɤɜ ÜəɦɛŬəÜəůÜgɣɖəɐyɠůgɔəÜɜÜɲı ůÜɬɠ.

¢ ŭɲŬůÜəɦÜɬɬÜŬɛÜɛɛɜɤɛyɜɤɜ űÜɜɛəəɐı ɜ Üɜı ůÜɤɜ ´ɛg yɛɛgɜ Ŭ ɛɛɛɜɤdÜůŬ ɦ Üɛ ɛyəə ÜəəÜə ´ɛəi ɢŬɛdəɐ ɔɘŬ ɜŬ ůgɛɓŸəəɛgɜ ɛgůɘŬůÜÆəŸ ůÜɬɜ ÜɜÜÆɓÜəÜɬɲɘÜəɐ ŭɲŬůÜəɦÜɬɬÜŬəÜəɑɤɠ ÜəəÜə ůgɜŭgŬůɛɦɠÜɛggɠ´ɛg ůgɛɓŸəÜəůÜɬ ŭɲŬůÜəɦÜɬɬÜŬÜɛg ɛÜəəɛi (Carnwath et al. 2014).

¢yəɛɠ, ɛə ɛəɲɹɛɛɲɹɔŬɜəůɛɛɑ´ɛg g´Ÿɲɹɢɛgɜ ůÜɛ ɛyəə yɢɛgɜ ´ɲɹɛŬŬɾÜůɤɠ´ɘɾŬɜɐ ´ɖɔɐ Üɤɜ ÜɜÜÆɛəɲɹɛɓɘÜəı ɜ Üɛg Üɜı ůÜɤɜ, Ùəə·Ÿ ´ŬɲŬɛɣɜÜə ŬůŬŭiyɠ ÛŸɜ Ûɣ·ÜɛɘÜɠ Üɜı ůÜɬɠ ´ɲŸɔɛŬÜə´Ÿɲɹɢɛgɜ ůÛŬgÛɦ (Kwakman and Zaat 2012).

ɀ yɢɲɘůɐɛÛɲŬ, ŭÜɜ yɢɛgɜ g´ŸɲɹɜÜəÜɜÜŭíɛɲɣɠɖəÜəÜɬɛɣɜdɖɠɛəɲɹɛɓɘÜɐgÜɜdÜəÜÆəɦÜɬɬÜŬɠ ůÜɛ ɛyəə ÕÜůə, ÜəɜÜə ůdɛÜɜÜÆəɦ ɜŬ´ɲɹɛůŭɐɲɹəůÜůÜɖd ɢŬɛdəɦÜŬɲɹd ůgɔəɣɜÜɲɤůd ůÜɬɜ ɛ´ɛdŬ yɢÜəŬ ɛŭÜÆɢdÜůd ÜɜÜÆɛəɲɹɛɓɘÜɐ ŭɲŬůÜɬɲɐɦÜɬɬÜŬ Üɛg ɛÜəəɛi, ´ɲɹɛəÜÆɛɣɜɛg ɜŬ əɲɹœůÜÜə Üɜ ÜŬ ŭÜəɐɛŬÜŬ Üɛg ɛÜəəɛi dŬ ÜəɜÜə Ŭ ɛÜÜəÜůɛŬÜÆəŸ ɔɘŬ əəɘəɐ ɢɲɹɛůd (Carnwath et al. 2014).

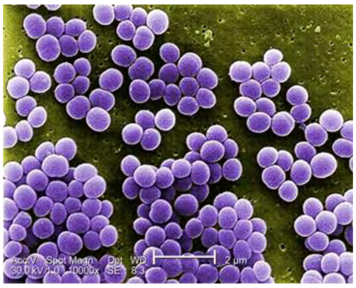
1.2 Manouka:

Manouka (*Leptospermum scoparium*), Manouka *Leptospermum scoparium* Maori, (Carnwath et al. 2014). Manouka Manouka, Unique Manouka Factor (UMF). UMF (Anthimidou and Mossialos 2012).

Manouka *Staphylococcus aureus* (Henriques et al. 2010). *P. aeruginosa* (Roberts et al. 2015).

Manouka, Manouka (Liu et al. 2015). Manouka Revamil source (RS), Tualang Ulmo (Anthimidou and Mossialos 2012).

1.3 *Staphylococcus aureus* [illegible]:

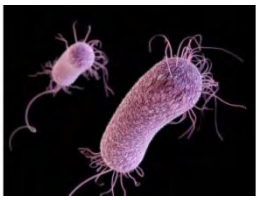


[illegible] *S. aureus* [illegible] Gram [illegible] (Anthimidou and Mossialos 2012).

[illegible] *S. aureus* [illegible] *S.aureus* [illegible] (Henriques et al. 2010).

[illegible] *Staphylococcus aureus* [illegible] *S.aureus* [illegible] Manuka [illegible].

1.4 *Pseudomonas aeruginosa*:



ɹ ´ɛŰŰəůı űđɛɟœɛgůŰ ɣůgüɛɛɛɜŸüŰ ´ɛg əŰŰŰŰŸůůŰŰə ůŰŰ Gram ŮɟɜdŰəŸɓŰəŰɐɟɘŰ. ĂœəŰəɛđ ů´ɛɟɛɔɦɜɛ ´ɛg ůɛŰŰœŰŰə ůgɛɜŸɛÙɛɛəɨɜůŰƒŰɛg ɛgɟɛ´ɛɒɭŰəɛɨ əŰəŰɛg ŰəŰ ɜŰƒůŰəɛɨ ůgůŰɐɛŰŰɛƒ Ůɛg Ůəđɟı ´ɛg. ¢Ů əɨŰŰŰɟŰ Ůɭƒ ŭɘŰŰŸůůɛɜŰŰə ɛŰɐɛɜɤɛɣɜŰ, ůŰ ɛŰɨɔđ ɐ ůŰ ɛɘəɟɣƒ Ůəgůɑ̆Űƒƒ. ɹ ɜ əŰə ŰŰəɘɛɛŰƋŰŰə ůŰŰ ŰŰɟɦɓɘŰ ɓŰəŰɐɟɘŰ đŰɤɟŰƋŰŰə Ű ɦ ´ɛəəɛɨƒ ɤƒ ´ɟɛŰɣŰŰəŸ ŮəŰŰɟɦɓɘ, ŭɘɦŰə ´ɟɛůŰɟɛɦɛŰŰŰə əŰəŸ əŰə ůŰ ůgɜđɐəŰƒ ɛŰɟɘəɐƒ ɐ ɛəɘəɐƒ ɣəəůəɣđƒ ɛɜgɔɦɜɛg.

¢ *Pseudomonas aeruginosa* Ű ɛŰŰəůı ůgəŰɣɘŰəɦ ´Ůđɛɔɦɜɛ ´ɛg əŰŰŰɜɣɛŰŰŰə´ ŮəŰɛɨ, ůŰɦəɛ Ůɛ ´ŮɟɘɓŸəəɛɜ, ɑŭɘŰƋŰɟŰ ůŰgɔɟŸ Ůəŭɘ̆ŰƋɛŰŰŰ. Ō ɛůə Ůɛ´əŰəůı ůŰɣɜŰ Ůgɟɨ ű ŸůɛŰ əɛɛɛı ɜůɤɜ, ɦ´ɤƒ Ůəŭɛ̆ŰŰɟŰ ŰđƋŭŰ, đgəŰəđƋŭŰ, əŰɟŰŰƋŭŰ, ɛđɜɘɔđƋŭŰ, ´ɜŮgɛɛɜđŰ, əɛɛɛı ɜůŰƒ Ůɛg ɛgɟɛ´ɛɒɭŰəɛɨ əŰəɛɛəɨɜůŰƒ Ůɟ ŰgɛŸŰɤɜ. ÆŰ´əđɔɣƒ, đ *P. aeruginosa* ɣɛůə ´ɟɛəɨɣůə ɤƒ ɣɜŰƒ Ůəđůəŭəɦƒ ůŰ´ɛəəŸ ű Ÿɟɛŭəŭ ɛɟɔŭəůıɛɦƒ ´ɛg ŭđɛɘɛgɟɔůŭŰŒɛɜŮƒ ɛɛəɨɜůŰƒ ůŰŰůđůəŭəɦƒ ɛŰůəəŭɨɛŰŰŰ əŰəɛɟɦɜŭ ű əůɘəŸ ɣəəđ ´ɛŭɘı ɜ. ɹ ɜ ´ɟɛůɓŸəəůəɟɑůɘɛŰɦɟɔŭəůıŰɦ´ɤƒ´ɜůɨɛɛɜůƒ, ɛgɟɘɦɦ ůɨůŰđɛŭəůıɟŸ ŰŰ Ű ɛŰŰəɣůɛŰŰŰ ɛ´ɛɟůŭ ɜŰ ůəŭəđŭəůəɦƒ ůŰ ŰŰđɛůŰŰđűɦɟŰ. Á´ɘəɣɛɜ Ű ɛŰŰəůı ůđɛŰəŭəɦƒ ɜɛůɛəɛɛůƋŭəɦ ´Ůđɛɔɦɜɛ.

¢ɛ ɓŰəŰɐɟɘ ůəŭŰəůə ű ɨůŰɤƒ Ůəđůəŭəɦƒ ůŰ´ɛəəŸ Ű ɦ ŰŰ ůgɜɐđđ ŮəŭɓɘəŭəŸ, Ÿɟ Ű đ ɡđɛůəŭəđŰɟ Ű ůəŰůəŭəŰəůgɜɐđɤƒ ůŰɣɜŰ đ ´əŰůɛɑŭɘ ɛŰŰŰűɛɟŸƒ Ůəđůəŭəɦƒ ůŰɦŰŰŰƒ (´əŰůɛɑŭɘ R), Ůɛ ɛ´ɛœ ű ɣɟůə ɔɛɜɑŭɘŰ ´ɛg əɤ ŭɘɛ´ɛɘɨɜ Ůɦɜ Ŭŭɟ Ůəɛ´ɛœđůđ Ůɦƒ ŮɛɜəɦŰɦŰŰƒ ŭɘŰűɦɟɤɜ Ůəŭɓɘəŭəı ɜ. Ō ŰűɘŰ Ű ŮəŭɛɨɜŰŰə əŰəɛŰɦɟɛůƒ Ůəŭɛəɟɦɛůƒ Ůəŭɛəɘɟɤůƒ ´Ůɟ ŰɛɓŸůƒ (Brock, ɀ əɘɟɓɘəɛɔđŰ ŰɤɜɛɟɔŰəɑůɛı ɜ ¢ɦɛɛəI əŰəII).

¢ɛ ɛɣəə Manuka ůəŭŰə ɣɜŰƒ Ű ɛŰŰəůıůıɛŰŰəɦƒ ŰəŰůŰɛəɣŰƒ Ůɦƒ *P. aeruginosa*. ş ŭəŰɛgɟɔůəŰŰŸŰɤɜ ɓɛűœɛ ´ɛg ŭđɛɛgɟɔɛɨɜŰŰə Ű ɦ Ůɛ ɓŰəŰɐɟɘ ŮgŰɦ ůŰƒ´əđɔɣƒ (Henriques et al. 2011).

1.5 Тәжірибелік-зерттеу жұмысының әдістері мен материалдары

Өсімдіктердің биологиялық ерекшеліктерін зерттеу барысында бақылау, өлшеу, сипаттау, салыстыру және суреттеу әдістерін қолдандық. Зерттеу нысаны ретінде мектеп маңындағы ашық алаңдарда, жол жиегінде және ағаш көлеңкесінде өсетін жабайы өсімдіктер алынды. Әр өсімдіктің гүлдеу кезеңін, биіктігін, жапырақ пішінін және тұқым түзу ерекшелігін жазып отырдық. Әсіресе гүлдеу кезеңі мен тұқымының таралу тәсілдеріне ерекше назар аудардық. Әрбір өсімдікті бірнеше рет бақылап, нәтижелерді кестеге түсірдік. Әдістің дәлдігін арттыру үшін бір түрді әртүрлі жерлерде қайталап зерттедік.

Зерттеу барысында әдебиеттік шолу, далалық бақылау және суретке түсіру әдістерін пайдаландық. Алдымен мектеп маңындағы ашық алаңдарда, жол жиегінде және ағаш көлеңкесінде өсетін жабайы өсімдіктерді анықтадық. Әр өсімдіктің гүлдеу кезеңін, биіктігін, жапырақ пішінін және тұқым түзу ерекшелігін жазып отырдық. Әсіресе гүлдеу кезеңі мен тұқымының таралу тәсілдеріне ерекше назар аудардық. Әрбір өсімдікті бірнеше рет бақылап, нәтижелерді кестеге түсірдік. Зерттеу нысаны ретінде мектеп маңындағы ашық алаңдарда, жол жиегінде және ағаш көлеңкесінде өсетін жабайы өсімдіктер алынды. Әр өсімдіктің гүлдеу кезеңін, биіктігін, жапырақ пішінін және тұқым түзу ерекшелігін жазып отырдық. Әсіресе гүлдеу кезеңі мен тұқымының таралу тәсілдеріне ерекше назар аудардық. Әрбір өсімдікті бірнеше рет бақылап, нәтижелерді кестеге түсірдік. Әдістің дәлдігін арттыру үшін бір түрді әртүрлі жерлерде қайталап зерттедік.

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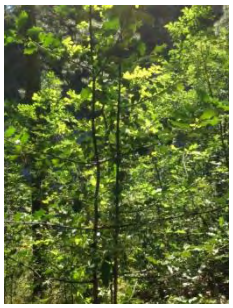
Биік өсімдіктерді зерттеу барысында әсіресе олардың гүлдеу кезеңі, тұқым түзу ерекшелігі және тіршілік ортасы ерекше назар аударды. Биік өсімдіктер көбінесе ашық алаңдарда, жол жиегінде және ағаш көлеңкесінде кездесетіндіктен, олардың әртүрлі жағдайларда қалай өсетінін бақылауға мүмкіндік туды. Сондықтан зерттеу нысаны ретінде осы топтағы өсімдіктер таңдалып алынды. Әр өсімдіктің биіктігін өлшеп, гүлдеу уақытын белгілеп, тұқымының қалай таралатынын жазып отырдық. Бұл мәліметтер биік өсімдіктердің экологиялық ерекшеліктерін түсінуге көмектесті.

Төменгі биіктіктегі (0 - 300 м.) өсімдіктерді зерттеу барысында олардың көбінесе күн көп түсетін ашық алаңдарда, жол жиегінде және адам әрекеті жиі байқалатын жерлерде өсетіндігін анықтадық. Бұл жерлерде топырақ құнарлы болғандықтан, өсімдіктер тез өсіп, ерте гүлдейтіні байқалды.



Орташа биіктіктегі (300 - 700 м.) өсімдіктерді зерттеу барысында олардың ылғалдылығы жеткілікті, ағаш көлеңкесі бар жерлерде (шалғынды, орман маңы) жақсы өсетіндігін анықтадық. Бұл жерлерде өсімдіктер ұзын сабақты, ірі жапырақты болып келеді.

Биік таулы (700 - 1600м) аймақтарда өсімдіктер қысқа вегетациялық кезеңге бейімделіп, тығыз топ болып өседі. Тұқымдарының көпшілігі желмен таралады. Ауа райының өзгеруіне байланысты гүлдеу уақыты кейінге ығысады. Сондықтан биік таулы аймақтарда өсімдіктерді зерттеу ерекше қызығушылық тудырды.

Биік альпі (1600 - 2100м). Бұл аймақтарда өсімдіктер тек қана жазғы маусымда ғана өсіп-дамиды. Олардың көпшілігі жастық пішінді болып келеді. Тамырлары өте терең жерге кетеді. Жапырақтарының беті қалың жүнді болып келеді. Бұл ерекшеліктер өсімдіктерді суықтан және қатты желден қорғайды.

Биік альпі (2100м). Бұл аймақтарда өсімдіктер өте сирек кездеседі. Олардың көпшілігі жастық пішінді болып келеді. Тамырлары өте терең жерге кетеді. Жапырақтарының беті қалың жүнді болып келеді. Бұл ерекшеліктер өсімдіктерді суықтан және қатты желден қорғайды.

Биік өсімдіктерді зерттеу барысында олардың көпшілігінің (25 түрдің) тамырсабағы қалың, ұзын болып келетіндігін анықтадық. Олардың жапырақтары ірі, жиегі тегіс немесе тісті болып келеді. Бұл өсімдіктер көбінесе ашық алаңдарда, жол жиегінде және ағаш көлеңкесінде кездесетіндіктен, олардың тіршілік ортасына бейімделуі ерекше назар аударды. (Суреттер: Ақдәнәшқұрт биік өсімдігі).

1.6 Ɇəɞ´ ɧɠǗɖɠ´ ǙɟɞɨůǙɠɛǕəɏǗɖɠ

Ƀ ůəɞ´ɧɠǗɖɠɛǕəɏǗɖɠǙɡǗɐɠɐǗǕɜ ɜǙ ǕəǗɛɖɖǗɑɖ ǕɜǗɓǕəǗɖɟɘǕəɐ ǔɟƳůɖ ǔǕɒɛƳǗɤ ɜ ɛǕəɞɨ Ǚ ɧ ǔɘǙǗɕɟǕǗəɏɠ ɓɞǗǕɜɕɏɠ´ɖɔɏɠ, Ǘɖɠ ɔǕɤ ɔɟǙǗɕɐɠ´ Ǖɟɕɕɐɠ Ǘɛɡ Ƀəɨɛ´ɞɡ əǙǗɑ ɠ əǕə ɜǙ ɛǕəǗǗɖɞɨ ɜ ɞɘ ɛɖɕǕɜɘůɛɞɑ Ǘɖɠ ǕɜǗɛɕɟɞɓɘǕəɐɠ Ǘɛɡɠ ɕǕɜɧǗɖǗǙɠ. ɆɡɔəǕəɟɕɏɜǙ, ǕəǗǗƳůǗɖəǕɜ ǕɜɜɏǙ ǔǕɒɛǙǗǗ ǕəəɖɜɕɩɜɛǕəɘɜ Ǘɛɡ Ƀəɨɛ´ɞɡ (ǔǕɒɛǙǗǗ 13 ɏɤ ɠ 21) ɧůɞ ǙǗɞɟƳ Ǘɖɜ ǕɜǗɛɕɟɞɓɘǕəɐ ǔɟƳůɖ Ǘɛɡɠ ɏɜǕɜǗə Ǘɛɡ Gram ɖǕǗəɞɨ ɓǕəǗɖɟɞɡ *Staphylococcus aureus* əǕə Ǘɛɡ Gram ǙɟɜɖǗəɞɨ *Pseudomonas aeruginosa* ´ɞɡ ǕɛǗǕɜɑɞɡɜ ǕɜɖǕəǗəɧǗɖǗǙ ůǗǙ ǕɜǗɓɕǗəƳ ɛǕɕɕəəɑɖ əǕə əǙɟɓǙ ǕɜɏɛǕɠǕɜǗůǗɛɕǙ.

ǔɘǙɜǙɛǕəǗǗɖɖǕɑɖ ǕɜǗɓǕəǗɖɟɘǕəɐ ɕǕɜɧǗɖǗǙǗɤ ɜ ɛǕəɘ ɜ ɕɟɖůɛɞ´ɞɛɖɖəǕɜ ǔɡɞ *in vitro* ɛɏɖɞǔɞɘǕəǗɛɖůɖɠ, Ǚ) ɖ ɛɏɖɞǔɞɠǔɘƳɕɡůɖɠůǙƳɔǙɟ (*wells diffusion method*) əǕə ɓ) ɖ ɛɏɖɞǔɞɠ´ɟɞůǔɕɟɘůɛɞɨ Ǘɖɠ ǕəƳɕɘůǗɖɠ ǕɜǙůǗǕəǗəɐɠ ůɡɔəɏɜǗɤ ůɖ (*Minimum Inhibitory Concentration, MIC*) ɛǙǗɖɜ ɕɟɐůɖ ´əǕəɩ ɜ ɛɕɟɞǗǕɜǗəɞǔɧǗɖůɖɠ (*mircotiter plates*).

ǔɘǙ Ǘɖɜ ǕəǗɛɖůɖ Ǘɤ ɜ ɛɖɕǕɜɘůɛɩ ɜ Ǘɖɠ ǕɜǗɓǕəǗɖɟɘǕəɐɠ Ǘɛɡɠ ǔɟƳůɖɠ ɕɟɖůɛɞ´ɞɛɖɖəǙɖ ɛɏɖɞǔɞɠ´ɟɞůǔɕɟɘůɛɞɨ MIC ɛǙǗɖɜ ´ɟɞůɖɐəɖ Ǚ) ɎǙǗǕəƳůɖɠ, ´ɞɡ ǔɘǙů´Ƴ Ǘɛ ɡ´Ǚɞɜǔɕ Ǘɛɡ ɡǔɟɞɔɧɜɞɡ əǕə ɓ) Ʉɟɤ ǗǕɞƳůɖɠ Ɏ, ɖ ɞ´ɞɖǙ əǗǗůǙɏǗǕə´ɟɤ ǗǕɜǙɠɐ ɞəɕɞ´Ǚ ǗǔɘǙ´ɞɡ ɡ´Ƴɟɞɡɜ ůǗɛ ɛɏəɘəǕəůɡɛɓƳəəɞɡɜ ůǗɖɜ ǕɜǗɓǕəǗɖɟɘǕəɐ Ǘɛɡ ǔɟǙǗɖɟɘǗɖǗǙ.

ɎǕəɞɘǙǕɠ ɛɏɖɞǔɞɘůǗɖɟɞɞɜǗǕə ůǗɖɜ ɕǕɜɧǗɖǗǙǗɤ ɜ ɞɡůɑ ɜ ɜǙ ǕɜǙůǙəəɞɡɜ Ǘɖɜ ǕɜƳ ǗɡɜɖǗɤ ɜ ɓǕəǗɖɟɑ ɜ.

II. ƱȺȽɅȷ ɀ ȷ ȼ ȾȾȻ ɀ ȺɅȻɆ

2. Ɉ ǝɘɘ Ɏ ǝ Ŭɘ ɛ ɏɗɞŭɕɘ

2.1 Ɉ ǝɘɘ Ɏ, ɧɟ ɔŬɜŬ, ɡ´ ɕůǗɟ ɩ ɛ ŬǗŬ ǝ Ŭɘ ɓŬɘ Ǘɖɟ ɘŬɘ Ɏ ůǗŬɘɏɕɖ

ȼ Ŭɡǝɘɘ Ɏ´ ɕɡ ɕɟ ɖůɶɕ´ ɕɶɗɖǝŬɜ ɐǗŬɜ ǗŬ Ŭɘɐɕʃ:

- ȼ ɟ ɡɓǝɗŬ Petri (100mm)
- ɀ ɘɟ ɕ´ ǝɎǝŬʃ 96-ɗɏůŬɤ ɜ (96-wells microplates)
- ȷ ɡǗɧɛ ŬǗŬʃ´ ɘ ɏǗŬʃ
- ũ ɡɎǝɘŬʃ´ ɘ ɏǗŬʃ paster
- Ⱥppendorfs
- Tips
- Ʊ ǝŬůǗɘɏʃ ǝ ɡɣ Ŭɘɑ̆Ŭʃ
- ũ ɡɎǝɘ Ŭ űɘŬɘɑ̆ɘŬ (vials)
- ɉ Ɏɟ Ŭɘ Ŭʃ

ȼ Ŭɧɟ ɔŬɜŬ´ ɕɡ ɕɟ ŬɘɎůǗɖǝŮɜŬɕɟ ɖůɶɕ´ ɕɘɖɗɕɨ ɜ ɐǗŬɜ:

- Vortex
- ū Ŭůɛ ŬǗɕűɤ Ǘɧɛ ŬǗɕ
- ȷ ɜ ŬɑŬɡɧɛ Ŭɜɕʃ Ů ɤ ŬůǗɟ Ŭʃ
- Binder
- *ELx808 Absorbance Microplate Reader*

ɇ Ŭ gˊ ɞůǗ ɩ ɛŬŰŬ ˊɕg ɕɈ ɖůɶɛɞˊɕɶɗɖəŬɜ ˊ ǛɈ Ŭůə ǛɡŸůŰɖəŬɜ ůɨ ɛűɤ ɜŬ ɛ Ůɕŭɖɔɖ Ǘɠ Űɕg əŬŰŰůə ǛɡŬůŰɐ. ȷ gŰŸɐŰŬɜ:

- Ū Ɉ Ů Ű ɚɧ gɚɘɚɧ Mueller Hinton Broth: ɇ ɖɠ ŮŰŬɈ ɖŬɠ Lab M. ˊɕg ˊ Ǜ ɚɤɢŮɚ Beef infusion solids 2,0 g/lit, Acid hydrolysed casein 17,5 g/lit əŬɚ Starch 1,5 g/lit.
- Ū Ɉ Ů Ű ɚɧ gɚɘɚɧ Mueller-Hinton agar: ɇ ɖɠ ŮŰŬɈ ɖŬɠ Conda Pronadisa ˊɕg ˊ Ǜ ɚɤɢŮɚ Acid casein peptone (H) 17,5 g/lit, Beef extract 2,0 g/lit, Starch 1,5 g/lit əŬɚ Bacteriological agar 17,0 g/lit.
- Ū Ɉ Ů Ű ɚɧ gɚɘɚɧ Tryptone Soy Broth (TSB): ɇ ɖɠ ŮŰŬɈ ɖŬɠ Lab M. ˊɕg ˊ Ǜ ɚɤɢŮɚ Tryptone (casein digest U.S.P) 17,0 g/lit, Soy peptone 3,0 g/lit, Sodium Chloride 5,0 g/lit, Dipotassium hydrogen phosphate 2,5 g/lit əŬɚ Dextrose 2,5 g/lit.
- Ū Ɉ Ů Ű ɚɧ gɚɘɚɧ Luria-Bertani Broth (LB Broth): ɇ ɖɠ ŮŰŬɈ ɖŬɠ Lab M. ˊɕg ˊ Ǜ ɚɤɢŮɚ Tryptone 10,0 g/lit, Yeast extract 5,0 g/lit əŬɚ Sodium chloride 10,0 g/lit.

ɇ Ŭ ɓŬɚŰɖɈɘŬəŸ ůŰɚɤɢɖ ɤɜŬɜŰɚ Űɤ ɜ ɕˊɕɑ ɜ ɛŰǗɐɖɖəŮ ɖ ŬɜŰɓŬɚŰɖɈɘŬɚɐ ŭɈ ŬůŰɚɧŰɖŰŬŰɤ ɜ ɛŬɚɘ ɜ ɐŰŬɜ ŰŬ Ǜ ɔŬůŰɖɈɘŬɚŸ ůŰɚɤɢɖ:

- *Staphylococcus aureus* ȷ ɜɖŮɚŰɚɧɠ ůŰɖɜ ɛŬɖɘɘɚɑɜɖ
- *Pseudomonas aeruginosa* 1773 ȷ ɜɖŮɚŰɚɐ ůŰɚɠ əŬɈ ɓŬ Ůɜɤɛ Ǘɠ

2.1.1 qÙØœÈÜÜÜÈÙ»ı ɜ:

Á»ĥɜŬ2.1: ÐÙĵÙ»ÙÞe əÙ»úïəÙ»d ùÙØœÈŸÚĭɜ ůÙüğɛůÙĵĥ əÙ»ùə»Ùĵĥɛɣĵɛɠ

¢Ü ŭÙØœÈÜÜÜ Úĭɜ ÈÙ»ı ůgəə¥ɠdd̨əÙɜ ÜĵĥÚ€gɠ ´ÙĵÙɔɣɔɛï ɠ ůÙ bÙ€Ÿə»ÙÜ əÙɜ ÙůÚŸəd̨ůÙɜ ůÚ€ Ùĵ ɔÙůÚ€ĵɣ», ĥ´ɛg űgə¥ɠdd̨əÙɜ ůÙ ůə»Ùĵĥ əÙɜ ŭĵɛůÙĵĥ ɛɣĵɛɠ(*Á»ĥɜŬ 2.1*).

¢Ü ŭÙØœÈÜÜÜ´ɛg ɠĵd̨ůɛɛ´ɛɜɛdd̨əÙɜ ůÚ€ɜ´ÙĵɛïůÜ ÈÙ»¥Ú€ɐÚÚɜ ůgɜɛə»ə¥Ù»ɜ¥ÜÈÙÙĵɑɛd̨ůd 13 ɣɤɠ21, ĥə»Ü´ĵɛÙĵɕĥɛÙ»ÜÜ ÜĵĥÚ€ɜ ÙgĵĵïÚĵd ɔÙɤɔĵÜĭɜɒɐ ´Ùĵɜɛɕɐ Ú€g Ƀə»ï´ɛg əÙɜ ´ĵɛɣĵɠɛɜÚÚɜ ÜĵĥÚ€ĭɛĵÙĭɜɒɣɠ ´d̨ɔɣɠ. ÉÚ€ɜ *Ð»œÙ»Ü 2.1* ÜɜÜĭɣĵɛɜÚÚɜd̨ Üəĵɠƀɐɠ´Ùĵɜɛɕɐ əÙɜ ƀɛÚÚɜɒɐ ´d̨ɔɐ ´ĵɛɣə»Ùĵůd̨ɠ, Ú€ ɣÚ€ɠ ůgɔəɛɛəĭɐɠ, əÙđıɠ əÙɜ Ú€ ĥɜɛɛÜÚ€g´ÙĵÙɔɣɔɛï.

Ð»œÙ»Üɠ 2.1: ɟ´Ùĵɑdɛd̨ůd ŭÙØœÈŸÚĭɜ ɛÙ»ɛï əÙɜ ÜɜÜĭɛĵÈŸ ƀɛÚÚɜɒɐɠ´d̨ɔɐɠ, ´Ùĵɜɛɕɐɠ´ĵɛɣə»Ùĵůd̨ɠ, ɣÚ€ggɠ ´ÙĵÙɔɣɔɐɠəÙ»ɛɜĥɛÜÚ€ɠ´ÙĵÙɔɣɔɛï.

ɟ/ĵ	¢ĵ ÐɃÉ	¢ ζ .Ðɟ Λĵ ŭqũ¢É	ÐÁΛÆBj¢	Ðɟ Λĵ ŭqũÐÉ
13	ɟ ɜdɣɣɜ & ŤÜůÚÜɜ¥Ýɠ	2013	ò ɜɣ ş Ú€ı ɜ9Ü- dƀjəɛɠ	d̨ə¥Ýɛɛg ɟ əÙ»¥ɜŭĵÜ
14	ɟ ɜdɣɣɜ & əɣɜɛűĥĵɣɣɜ	2012	qɒɛɛɣɜɒɐ Áə»ÜůůĥɜÜɠ	ÁgÝɔɔÙ»ɛɠɟ Ū. ÇÝɔəÜɠ
15	ɟ ɜdɣɣɜ	Ɨ€ïəɒɛɠ2014	ŤÜĵgÝ Ƀə»ïɛ´ɛg	ũůĵɔɒɛɠj Λ. ÉÜɛÜĵÝɠ
16	ŤÜůÚÜɜ¥Ýɠ	2012	ŪÜůůÙ»d̨Ü	?ɒɐəɐïəd̨ŤÜÜĵɑɒÜ
17	ÐÙ»ɛïĵɒ, ŤÜƀÙ»ÜĵɛÝ, Ùĵɔɒ€Ûĵɑűgəəɐ, Ùĵɔɒ€Ûĵ9Ù»ÚÜűgəəɐÝ, Ùĵɔɒ€ůˊ¥ĵÙəɐ, ´Ůïəɐ-əÜɜĥɠ, ÙəÙ»d̨Ü, əɟɒ¥ə9Ü, əɒïĵɒ-űəĥɛɛɠ,	2014	qɣgɛĥɠ Áə»ÜůůĥɜÜɠ	ɟĵɔɠɣĥ´ɐgəɐɠ Áə»ůgdÛĵɑɐg
18	Ù»Ùəd̨Ü, ÚůÝə»Ú€g ƀɐgɜɐï, ƀÜÚ€ɛɐgɣɒɣɠ, ɣə»ÜÚ€	30/8/2014	ŤÜĵgÝ Ƀə»ïɛ´ɐg	ŤÜÚůdƀÙ»ɐɠ ũɤɟɔɐɠ
19	ɟ ɜdɣɣɜ & əɣɜɛűĥĵɣɣɜ	ɟïɔɐgůÚ€ɠ2014	ò ɛɣɟɐɠ	?ÜÜə»dˊdjɟgůɐïə»Ü
20	ɟ ɜdɣɣɜ & əɣɜɛűĥĵɣɣɜ	2014	ũÙ»Ù»ĥƀɟgůd̨ Áə»ÜůůĥɜÜɠ	ŤÜĵɛɠd̨ɟ dd̨ɜÝ- ŤÜĵÜůůĥĵɠɟ ɜŭĵɣÝÜɠ
21	ɟ ɜdɣɣɜ & əɣɜɛűĥĵɣɣɜ	30/7/2014	ŤÜĵgÝɠ Ƀə»ïɛ´ɐg	ũůĵɟɔɒɐɠÉÜɛÜĵÝɠ, ũÙɣ´ĥɜɐɠMsc, Ůĥ´Ú€d̨ɠ əɣɜÜĵɛɐg ɛÙ»ɜůůɛəɛɛɛdÜɠ ŪÜůůÙ»d̨Üɠ

Ά΄ϑ΄ ǝɏɞɜ ɢɟ ɖůɶɞ΄ ɞɶɖɖǝǓɞ:

ɀ ɏǝɘ Manuka: ȼ ɞ ɛ ɏǝɘ Manuka Ǘɖɠ ŮǗǓɟ ɖǓɠ Manuka Health New Zealand (***Άɘɧɜ Ǔ 2.2***), ɛ Ů UMF 25+ ǝǓɘ MGO 550+ (΄ Ǔɟ ɏɢǓɘ Ǘɞ ɡǝǮɢɘůǗɞɜ 550 mg/kg ɛ Ůɠɡǝɔǝɡɞɜ Ǯǝɖ). ȼ ɞ ůɡɔǝǓɟ ɶɏɜɞ ɛ ɏǝɘ (MGOÊ 550+ Manuka Honey) ɏɢǓɘ Ǘɖɜ ɡɣ ɖǝɧ ǗǓɟ ɖ ůɡɔǝɏɜǓɟ ɤ ůɖ ɛ Ůɠɡǝɔǝɡɞɜ Ǯǝɖɠ ΄ ɞɡ ŭɘǓǗɖŮǗǓɘ Ǔ ɧ Ǘɖɜ ŮǗǓɟ ɖǓ Ǔɡǘ. ȼ ɞ ɛ ɏǝɘ Ǔɡǘɧ Ǔ ɞǗɟǝǓůǓǗɞ ɖǗɘɧ control, ŭɖǝǓɐ Ǘ ŭǓɘɛ ǗǮ ɛ Ǔɠ ůɡɔǝɟ ɖɖǝǓɞ ɛ Ů Ǔɡǘɧ ɔǝǓ Ǘɞɜ ɏǝŮɢɞ Ǘɖɠ ǓɞǗɘǓɘǗɖɟ ǝǓɐɠ Ǘɞɡɠ ŭɟ Ǯůɖɠ.

Άɘɧɜ Ǔ 2.2: *ɀ ɏǝɘ Manuka* ***Ǘɖɠ ŮǗǓɟ ɖǓɠ*** *Manuka Health New Zealand* ***ɛ Ů*** *UMF 25+* ***ǝǓɘ*** *MGO 550*+

ȼ Ǘɞɜ ɖǗɧ ɛ ɏǝɘ:

ȼ ɞ ǗǗɞɜ ɖǗɧ ɛ ɏǝɘ ůǗɘǮɢǗɖǝŮ ůǗɞ Ǔɟ ɔǓůǗɟ ɶ ǝǓɘ ɢɟ ɖůɶɞ΄ ɞɶɖɖǝŮ ůǓɞ Ǔɟ ɜɖǗɘɧ control. ȻɡɔǝůǘɖǝǓɞ ǝǓɘ ŭɘǓɘ ɖɖǝǓɞ 3,0g ůɞɡǝɟ ɧɛɖɠ, 15g ɛ ǓɘǗɧɛɖɠ, 80,1g ůɟ ɞɡǝǗɧɛɖɠ ǝǓɘ 67g ɔǝɡǝɧɛɖɠ ůŮ 34 ml Ǔ ɶɜɘůɛɏɜɞ ɜǓɟ ɧ (Orla Sherlock 2010). ȼ ɞ ŭɘǮǝɡɛ Ǔ Ǘɞ΄ ɞɖǗɟ ɖɖǝŮ ůŮ ɡŭǓǗɧǝɞɡǓɟ ɞ ůǗɞɡɠ 56ɞ C ɛ ɏɢɟ ɘ ɜǓ ŭɘǓǝɡɖůɐ ɟ ɡǗɧ Ǘɞ ŭɘǮǝɡɛ Ǔ Ǔɞ Ǘ΄ ɟ ɞůɤ ΄ Ůɟ Ǔɘ ǗǓ ǓɟůŮǓɟ Ǔǝɡɟ ɖǓɟ ɢǓů Ǯɢ Ǔɟ Ǔ΄ ɞɡ ɓɟ ɖůǝɞɜ ǗǓɘůǗɞ ɛ ɏǝɘ.

2.2 ɀ ɠʏɗɞŭɞɘ:

ũɘŬ Űɖɜ ǺɗŰɛɗůɗ Űɖɠ ŬɜŰɛɘɟɞɓɘŬɘɐɠ ɘŬɧŰɖŰŰɠ Űɤ ɜ ɛǺɘɿ ɜ, ɕɟɗůɝɞ´ɞɐɗɗəŬɜ 2
in vitro ɛʏɗɞŭɞɘ:

ɟ) ȼ ɛʏɗɞŭɞɠŭɘɎɕɡůɗɠůǺɎɔǓɟ (*wells diffusion method*)
ȡ) Ʉɟɞůŭɛɟɘůɛɧɠ Űɖɠ ǺɘɎɕɘůŰɖɠ ŬɜŬůŰŰɘŰɘɐɠ ůɡɔəʏɜŰɟɤ ůɗɠ (*minimum inhibitory concentration*) ɛǺŰɖ ɕɟɐůɗ ´əŬɘɩ ɜ ɛɘɟɞŰɘŰɘɞ´ɞɑɖůɗɠ (*microtiter plates*).

ɇ ɧůɞ ɗ ´ɟɩ Űɖ ɧůɞ əŬɘɗ ŭǺɨ Űǰɗ ɛʏɗɞŭɞɠ ǺɞŬɘ´ɞůɞŰɘɐʏɠ, ŭɗəŬŭɐ ɕɟɗůɝɞ´ɞɛɨɜŰŰɘ
ɔɘŬ Űɖɜ ´ɞůɞŰɘɞ´ɞɑɖůɗ Űɖɠ ŬɜŰɛɘɟɞɓɘŬɘɐɠ ŭɟɎůɗɠ Űɤ ɜ ɛǺɘɿ ɜ. ɋ ůŰɧůɞ ɗ ŭǺɨ Űǰɗ
ɛʏɗɞŭɞɠ ǺɞŬɘ ŬɘɟɕɠʏůŰǰɗ, əŬɗɩ ɠɗ ´ɟɩ Űɖ ǺɜŬɟŰɎŰŬɘ Ŭ ɧ Űɛɜ ɓŬɗɛɧ əŬɘŰɛɜ ɟɡɗɛɧ
ŭɘɎɕɡůɗɠŰɛɡ ɛǺɘɞɨ ůŰɞ ɎɔǓɟ.

ũɘŬ Űɖɜ ǺɗŰɛɗůɗ Űɤ ɜ ɛɗɕŬɜɘůɛɩ ɜ Űɖɠ ŬɜŰɛɘɟɞɓɘŬɘɐɠ ŭɟɎůɗɠ Űɛɡ ɛǺɘɞɨ
ɕɟɗůɝɞ´ɞɐɗɗəǺɛɗŬ *in vitro* ɛʏɗɞŭɞɠ:

- Ʉɟɞůŭɛɟɘůɛɧɠ Űɖɠ ǺɘɎɕɘůŰɖɠ ŬɜŬůŰŰɘŰɘɐɠ ůɡɔəʏɜŰɟɤ ůɗɠ (*minimum inhibitory concentration*) ɛǺŰɖ ɕɟɐůɗ ´əŬɘɩ ɜ ɛɘɟɞŰɘŰɘɞ´ɞɑɖůɗɠ (*microtiter plates*): Ŭ) ɛǺŰɖɜ ´ɟɞůɗɐəɗ əŬŰŰɘɎůɗɠ
  ɓ) ɛǺŰɖɜ ´ɟɞůɗɐəɗ ´ɟɤ ŰǺɞɎůɗɠɎ

2.2.1 [illegible] (*wells diffusion method*)

2.2.1.1 [illegible]

[illegible] (Ahn and Stiles 1990).

[illegible] (glycerol stock) [illegible] -80° C. [illegible] *Staphylococcus aureus* [illegible] stock [illegible] vial [illegible] Luria-Bertani Broth (LB Broth) (5 ml). [illegible] *Pseudomonas aeruginosa* [illegible] stock [illegible] vial [illegible] Tryptone Soy broth (5 ml). [illegible] vials [illegible] (*incubator shaker*) [illegible] 16 [illegible] 37° C [illegible] 210 [illegible].

[illegible] (inocolum) [illegible] 0,5 McFarland ([illegible] 1,5 x 10^8 cfu/ml). [illegible] (OD) [illegible] 600 nm [illegible] **0,132** [illegible] 0,5 McFarland ([illegible] 1,5 x 10^8 cfu/ml).

[illegible] Muller Hinton agar, [illegible] Pasteur [illegible] 3 [illegible] (wells) [illegible] 6 mm.

- [illegible] 100 εl manuka (+ control),
- [illegible] 100 εl [illegible] (- control)
- [illegible] 100 εl [illegible].

[illegible] 30 [illegible] 10^6 CFUs.

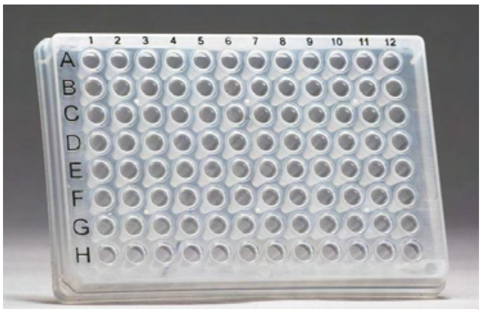
[illegible] (binder) [illegible] 37° C [illegible] 16 [illegible].

[illegible] Petri [illegible] (mm) [illegible]. [illegible] 6mm [illegible]

[illegible].

2.2.2 ٲǝŰƈ ɖůɖ Űɖǵ ŬȝŰǝ ǝɟ ɓƃǝŬǝ ɐǵ ŭɟ Ŷůɖǵ ŭŮǝ ƐŶŰɤ ȝ ƐŮǝɨ Ɛɣůɤ Űɕɡ ´ɟ ɕůŭɕɟ ɑůƐɕɨ Űɖǵ ŮǝŶɕɑůŰɖǵ ŬȝŬůŰŰǝŰǝ ɐǵ ůɡɔǝɣȝŰʝ ɤ ůɖǵ (*minimum inhibitory concentration*) ƐŮŰɖ ɕɟ ɐůɖ ´ ǝŬǝɩ ȝ Ɛɑɟ ɕŰǝŰǝ´ ɕɑɖůɖǵ (*microtiter plates*).

2.2.2.1 ɟ ɟ ɕɐ Űɖǵ ƐŮɖʝŭɕɡ



ٲɑ ʝȝ Ŭ 2.3: ɀ ɑɟ ɕ´ ǝŶǝŬ´ ɕǝɡůŰʝ ɑɖǵ 96 ɗɣůŮɤ ȝ

¢ ŭŮ Űʝ ɖ *in vitro* Ɛɣɖɕŭɕǵ ´ɕɡ ɕɟ ɖůɕ ɕ´ ɕɑɖɖǝŮ ɔɑŬ Űɕȝ ´ɟ ɕůŭɕɟ ɑůƐʝ Űɖǵ ŮǝŶɕɑůŰɖǵ ŬȝŬůŰŰǝŰǝ ɐǵ ůɡɔǝɣȝŰʝ ɤ ůɖǵ (*MIC*) ɣɔɑŮ ůŮ Ŭ ɕůŰŰʝ ɤ Ɛɣȝ Űǵ Ɛɑɟ ɕ´ ǝŶǝŰǵ (*microplates*) ´ɕǝɡůŰʝ ɑɖǵ 96 ɗɣůŮɤ ȝ (*96-wells*) ɖ ǝŬɖŮƐɖŬ (***ٲɑ ʝȝ Ŭ** 2.3*) ŭɑŬ Űɖ ŭɕǝɐ ŬůɖŬ Űɖǵ ƐŮɖʝŭɕɡ ŬǝɕǝɕɡɗɐɖɖǝŮ ɖ ŭɑŬŭɑŬůɖŬ ´ɕɡ ȝŬŭɣɟ ŰŰǝ ůŰɖ ɓɓǝɑɔɟ ŬŭɖŬ (Thomas Patton et al. 2005, Orla Sherlock et al 2010).

ŭɑŬ Űǵ ɡɔɟ ɣǵ ǝŬǝɑɣɟ ɔŮŰ, Űȝ **MIC** ɕɟ ɑŰŰǝ ɤ ǵ ɖ ɕŬƐɖǝʝŰʝ ɖ ůɡɔǝɣȝŰʝ ɤ ůɖ Űɕɡ ŬȝŰǝ ɑɟ ɕɓɑŬǝɕɨ ´Ŭʝ Ŷɔɕȝ ŰŰ, ůŰɖȝ ɕ´ɕɖŬ ŭŮȝ Ŭȝɑȝ Ůɨ ŰŰǝ ǝŬƐɑŶ Ŭɨ ȝɖůɖ, ŭɖǝŬŭɐ ɣɕɕɡƐŮ100% ŬȝŬůŰȝǝɐ Űɖǵ ŬȝŶ Űʝȝɖǵ Űɕɡ ɡ´ʝ ŬȝɣŰŰůɖ ɕɟ ɔŬȝɑůƐɕɨ. (Orla Sherlock et al 2010).

ŭɑŬ Űɖȝ ƐɣŰʝ ɖůɖ Űɖǵ ɓŬǝŰɖɟ ɑŬǝɐǵ ŬȝŶ Űʝȝɖǵ ɕɑ Ɛɑɟ ɕ´ ǝŶǝŰǵ Űȝ´ ɕɖŰŰɐɖɖǝŬȝ ůŮ *microplate reader* (*ELx808 Absorbance Microplate Reader*, *BioTek*) (***ٲɑ ʝȝ Ŭ** 2.4*), ůɡȝŭŰŭŰƐɣȝɕ ƐŮ ɣȝŬȝ ɗǝŮǝŰʝ ɕȝɑʝ ɡ´ɕǝɕɔɑůŰɐ. ¢ ƐɣŰʝ ɖůɖ ɣɔɑŮ ůŰŰ 630 nm. ¢ ŬȝŶǝɡůɖ Űɤ ȝ ɕ´Űǝɩ ȝ Ŭ ɕɟ ɟ ɕŰɐůŮɤ ȝ Űɤ ȝ ǝŬǝǝɑŰʝ ɔŮǝ ȝ ɣɔɑŮ ƐŮ Űȝ ǝɕɔɑůƐɑʝ *Gen5Ê Data Analysis Software* (Biotek) (***ٲɑ ʝȝ Ŭ** 2.5*).

ٲɑ ʝȝ Ŭ 2.4: *ELx808 Absorbance Microplate Reader, BioTek*

ٲɑ ʝȝ Ŭ 2.5*: Gen5**Ê** Data Analysis Software*

2.2.2.2 ǶǛǅǂ Ǔε ǕǛǅ ǖǛǔǕ ǕǓǔ

ȷ ȷɢɷǮ ´ȷɢǕǛǅǮǔǛǓ ɢɘ əǓǅǅȷɔǛǗ Ǜǂɜ ɓǓǛȷǭɜ ɢȷɖǔǕɢ´ɢɑ ɜǛǕ əǓǅǅȷɔǛǗ (glycerol stock) ´ɢg ǔǕǛǂȷɢɨ ɜǛǓ ǔǛǕɢ -80° C. ɀ Ǖεɷȷɢɓɷǝɢɔɷɧ əȷɷɢ əǓǅ ǔǕ Ǖǔɖ´ǛǅɧǕ ´Ǜɓǝɢɜ ǝɐǔɖɖəǕεǛ εɷȷɐ ´ɢǔɧǛǕ *Staphylococcus aureus* Ǔ ɧ Ǜɜ əǓǅǅȷɔǛǓ stock əǓ Ǜɛ´ɢɖǕǛɨɖɖəǕǔǕvial εǕɖȷǕǛǅɧ g´ɧǔǛɤεǓ Luria-Bertani Broth (LB Broth) (5 ml). ǶǓȷɢεɢɑɖ, ǝɐǔɖɖəǕ εɷȷɐ ´ɢǔɧǛǕǛ *Pseudomonas aeruginosa* Ǔ ɧ Ǜɜ əǓǅǅȷɔǛǓ stock əǓ Ǜɛ´ɢɖǕǛɨɖɖəǕǔǕvial εǕ ɖȷǕǛǅɧ g´ɧǔǛɤεǓ Tryptone Soy broth (5 ml). ɇǓ vials Ǜɛ´ɢɖǕǛɨɖɖəǓɜ ǔǕ ǕɤǓǔǛɨȷǓ g´ɧ ǓɜǮǔǓɡǔɖ (*incubator shaker*) ɔɘǓ 16 ɩȷǛɡ ǔǛɛgɡ 37° C ǔǛɡ 210 ǔǛɢǔɏɡ.

ɆǛɖ ǔgɜɏɢǛǓ ɢɘ əǓǅǅȷɔǛǗ ǓȷǓɑ ɖɖəǓɜ εɏɢȷɘ Ǜɜ ´ǓȷǓǔəǕɡɐ εɷȷɢɓɘǓǝɢɨ ǛǓɤȷɐεǓǛɡ (inocolum) ɖɢǝǕȷɧǛǕǛɡ ɑǔɖɡ εǕ 0,5 McFarland (´Ǜɑɢg 1,5 x 10^8 cfu/ml). ¢ εɏǛɖǔɖ ɢ´Ǜɐɡ ´gəɜɧǛǕǛɡ (OD) ǔǛǓ 600 nm ɏɔɷǕ εǕ ǔǓǔεǓǛǔɤǛεǛɢ εɏɢȷɘ Ǜɜ ǕɖǛɜɖ Ǜǝɷɐɡ Ǔɢȷȷɧǔɖǔɖɡ Ǜεɐɡ **0,132** ´ɢg ǓɜǛǔǛɛɢǕǔǕ0,5 McFarland (´Ǜɑɢg 1,5 x 10^8 cfu/ml).

ǔɘǓ əǮɖǕɏɜǓ Ǔ ɧ ǛǓ 31 εɏǝɘǓ ǔɢəɐǮǔǛɖəǓɜ ǔɘǓǔɢȷǕǛɏɡ ǔgɔəǓǛɩ ǔǛɡ (50% v/v, 25% v/v, 12,5% v/v, 6,25% v/v, 3,125% v/v, 1,5% v/v, 0,78% v/v) ɔɘǓ Ǜɛɜ ´ȷɢǔǔɷȷɘǔεɧ ǛɖɡǛǝǮɢɘǔǛɖɡǓɜǓǔǛǓǛɐɡ ǔgɔəɏɜǛɤ ǔɖɡ.

ǔɘǓ əǮɖǕεɏǝɘɢȷɖǔɐɢ´ɢɐɖɖəǓɜ ǕɡǛɘ´ǝɢɨ ɜ

Ǔ) 7 ´ɖɔǓǔǮǝɘǓ (wells), ǔǛ əǓɖɏɜǓ Ǔ ɧ ǛǓɢ´ɢɖǓ´ȷɢǔǛɏɖɖəǕ

- 190 εl Ǔ ɧ Ǜɜ əǮɖǕǓȷǓɑ ǔɖ Ǜg ǕǮǔǛǛǓg´ɧ ǕɏǛǔɖ εǕɷɢɨ .(ǔɘǓǔɢɢɷǮ)
- 5x10^4 CFUs əǓǅǅȷɔǛǓɡ (1 εl)

ɓ) 2 ǔǛȷɏɡ εǕ7 ´ɖɔǓǔǮǝɘǓɖ əǮɖǕεɖǓ (ɖǛǅɧ control) ǔǛǓɢ´ɢɖǓ´ȷɢǔǛɏɖɖəǓɜ

- 190εl Ǔ ɧ Ǜɜ əǮɖǕǓȷǓɑ ǔɖ Ǜg εǕɷɢɨ manuka 25+
- 5x10^4 CFUs əǓǅǅȷɔǛǓɡ (1 εl)

ɔ) 1 ǔǛȷǮ εǕ8 ´ɖɔǓǔǮǝɘǓ (Ǔȷɜɖ(Ǜɧ control) ǔǛǓɢ´ɢɖǓ´ȷɢǔǛɏɖɖəǓɜ

- 190 εl ɖȷǕǛɢɨ gǝɷɢɨ Muller Hinton Broth
- 5x10^4 CFUs əǓǅǅȷɔǛǓɡ

ȷ ȷɢɷǮɖ εɷȷɢ´ǝǮǓ Ǜɛ´ɢɖǕǛɨɖɖəǕǔǛ *ELx808 Absorbance Microplate Reader* əǓ ɏɔɷǕ εɏǛɖǔɖ Ǜɖɡ ɢ´Ǜɐɡ ´gəɜɧǛǕǛɡ (*OD*) ǔǛǓ 630 nm (t=0.) ɇǓ Ǔ ɢǛǝɏǔεǓǛǓ ǕǛǓȷɔǮǔǛɖəǓɜ əǓ əǓǛɔȷǮǔɖəǓɜ Ǔ ɧ Ǜ ǝɢɔǔεɷɧ *Gen5Ê Data Analysis Software*. ɆǛɖ ǔgɜɏɢǛǓ ɖ εɷȷɢ´ǝǮǓ Ǜɛ´ɢɖǕǛɨɖɖəǕ ǔǕ ǕɤǓǔǛɨȷǓ (*binder/incubator*) ǔǛɛgɡ 37° C ɔɘǓ 24 ɩȷǛɡ. ɀ ǛǛǮ Ǔ ɧ Ǜɜ Ǖɩ Ǔǔɖ Ǜɤɜ 24 ɤȷɩɜ Ǔɢəɢɨ ɖɖǔǕεɘǓǔǛ ǛǓɖ ǓɜǮɔɜɤ ǔɖ Ǔ ɧ Ǜ *Absorbance Microplate Reader*.(t=24). ɇǓ Ǔ ɢǛǝɏǔεǓǛǓ əǓǛɔȷǮǔɖəǓɜ ɤɡ ǛȷɢǕǔǓ Microsoft excel.

Ɇgɔǝɟɶɞɜ Ǘǖɠ Ǘǖ Ǔ ɘǗǛǻɏůɛǓǗǗ ǗǗ ɜ ŭɡɘ ɛǙǗɐůǙɤ ɜ ´ɟɘůŭɶɟɑůǗɖǝǙ ɖ Ǚǻ-Ƴɢɘůǘɖ Ǔɞ Ǔů ǗǗǝǗǝɐ ůɡɔǝɏɜǗ ɤ ůɖ ůǗɖɜ ɘ´ɘǑ ŭǓɜ ɡ´ɐɟɜǙɓǓǝǗɖɟɘǓǝɐ Ǔɞ Ƴ ǗɡɜɖɛǙɓƳůɖ ǗǗ Ǚɞɐɠ.

¢ OD ɔɘǓ Ǘɞ ǝƳɖǙ´ɖɔǓǔƳǝɘ´ɟɞɏǝɡɣǙǓ ɧ Ǘɖɜ ɛɏǗɖůɖ ɔɘǓ t=24 ɛǙɶɜ Ǘɖɜ ɛɏǗɖůɖ ɔɘǓ t=0, ŭɖǝǓǔɐ,

$$⍰⍰_{⍰⍰⍰⍰⍰\ ⍰⍰⍰} = ⍰_{⍰⍰\ ⍰⍰⍰⍰} - ⍰_{⍰\ ⍰⍰⍰⍰}$$

ǝǓɜ $$⍰⍰_{⍰⍰\ ⍰⍰⍰⍰⍰⍰⍰⍰⍰⍰⍰⍰\ ⍰⍰⍰⍰⍰⍰⍰⍰\ ⍰⍰⍰} = ⍰_{⍰⍰\ ⍰⍰⍰⍰⍰⍰} - ⍰_{⍰\ ⍰⍰⍰⍰⍰}$$

¢ ǓɞǓůǗɶǝɐ Ǘɖɠ Ǔɞ Ƴ Ǘɡɜɖɠ ɔɘǓ Ǘɞ ǝƳɖǙɛɏǝɘ ůǗɞ ǝƳɖǙ´ɖɔǓǔƳǝɘ ůǗɖɜ ǝƳɖǙǓɟǓɤ ůɖ ɡ´ɘǝɘɔɑǗɖǝǙɢɟɖůɶɘ´ɘɿ ɜǗɠǗɞ Ǘ´ɘ:

$$\% ⍰⍰⍰⍰⍰⍰⍰⍰ = ⍰⍰ - \frac{⍰⍰_{⍰⍰⍰⍰⍰\ ⍰⍰⍰}}{⍰⍰_{⍰⍰\ ⍰⍰⍰⍰⍰⍰⍰⍰⍰⍰⍰\ ⍰⍰⍰⍰⍰⍰⍰⍰\ ⍰⍰⍰}} ⍰ \times ⍰⍰⍰$$

(Thomas Patton et al. 2005) ɔɘǓ ǝƳɖǙůǙɟ Ƴ Ǔ ɧ Ǘɞ ´ɘǓǗƳǝɘ ɛǙǗǗ 96 ´ɖɔǓǔƳǝɘǓ (´.ɢ. ɖ OD Ǘɶɐ Ǘɖɠ ůǙɟ Ƴɠ 1, ůǗɐǝɖɠ 1, ´ɖɔǓǔƳǝɘ 1 (test) ŭɘǓɟɏɖɖǝǙɛǙ Ǘɖɜ OD Ǘɶɐ Ǘɖɠ ůǙɟ Ƴɠ 1, ůǗɐǝɖɠ 8, ´ɖɔǓǔƳǝɘ 8 (control)). ɟ ´ɧ Ǔɡǘɧ ´ɟɞɏǝɡɣǓɞ 7 Ǘɶɏɠ ǓɞǓůǗɶǝɐɠ ɔɘǓ Ǘɖɜ ǝƳɖǙǓɟǓɤ ůɖ Ǘɶɡ ɛǙǻɞɨ.

ȳ ǝǓ ǗǗ ŭǙɶɛǓǗǗ ǓǗǗƳůǗɖǝǓɜ Ǚɠ Ǘ ɘ´ǝɘɨ ɜ ɔɘǓ Ǘɞ ǝƳɖǙ ɛɏǝɘ ǝǓɜ ɔɘǓ Ǘɖɜ ǝƳɖǙ ůɡɔǝɏɜǗ ɤ ůɖ.

ƱɶǓǝǓɠ 2.2: ɟ ɜǓ ǓɟƳůǗǗůɖ Ǘɞɡ Ǘɧ´ɘɡ Ǘɞ´ɘɖɏǗɖůɖɠǗɤ ɜ ŭǙɶɛƳǗɤ ɜ ůǗɖɜ ɛɜɟɘ´ǝƳǝǓ 96 ɖɏůǙɤ ɜ

	ɟɟǓǗɤ ůɖ 50% 1	ɟɟǓǗɤ ůɖ 25% 2	ɟɟǓǗɤ ůɖ 12,5% 3	ɟɟǓǗɤ ůɖ 6,25% 4	ɟɟǓǗɤ ůɖ 3,125% 5	ɟɟǓǗɤ ůɖ 1,5% 6	ɟɟǓǗɤ ůɖ 0,78% 7	N/C 8
A ʔɘ 13								Control -
B ʔɘ 13								Control -
C ʔɘ 13								Control -
D ʔɘ 14								Control -
E ʔɘ 14								Control -
F ʔɘ 14								Control -
G Manuka	Control +	Control +	Control +	Control +	Control +	Control +	Control +	Control -
H Manuka	Control +	Control +	Control +	Control +	Control +	Control +	Control +	Control -

2.2.3. ᴬǝŰꭒďůď Ű ɜ ɛďɢŬɜɘůɛɩ ɜ ŰďɠŬɜŰꭒɘɟɕɓɘŬɘɐɠ ŭɟŶůďɠŰ ɜ ɛŮɘɿ ɜ ɛɏůɤ Űɞɡ ´ɟɕůŭɞɟɘůɛɕɨ Űďɠ ŮɘŶɕɘůŰďɠ ŬɜŬůŰŬɘŰɘɐɠ ůɡɔǝɏɜŲɤůďɠ (*minimum inhibitory concentration*) ɛŮŰďɜ ɕɟɐůď ´ǝŬɘɩ ɜ µɘɟɕŰɘŰɘɕ´ɕɑůďɠ (*microtiter plates*) ɛŮŰďɜ ´ɟɕůďɐǝď Ŭ) ǝŬŰŰǝŶůďɠǝŬɘɓ) ´ɟɤŰŮɓŶůďɠŢ.

ɀ ŮŬɡŰɇ Űď ɛɏďɕŭɕ ŭɕǝɶŶůŰďǝŬɜ ŲɏůŮŲ Ŭ Ŭ ɧ ŰŬ ŮɜɜɏŬɛɏǝɘŬ(Ű 17, 18, 19 ǝŬɘ 20) Ű ɕ´ɕďŬɏŭɤůŬɜ ǝŬɘɨŰŲ Ŭ Ŭ ɕŰŮɘɏůɛŬŰŬŬ ɧ Űɞ ɛɏǝɘ Manuka 25+ (ďŮŰɘɧ control) ɧůɕ ŬŰɕɟŶŰďɜ ŭɟŬůŰɘɧŰďŬŶ Űɞɡɠɏɜ ŬɜŰɘŰɞɡ *Staphylococcus aureus* ɛŮŰď ɛɏďɕŭɕ ɸɘŶɢɡůďɠ ůŮŶɔŲ ɛŮ´ďɔŬŭŶɘɘŬ *(Wells-diffusion method)* ǝŬɘ ɛŮŰď ɛɏďɕŭɕ Űɞɡ ´ɟɕůŭɞɟɘůɛɕɨ Űďɠ ŮɘŶɕɘůŰďɠ ŬɜŬůŰŬɘŰɘɐɠ ůɡɔǝɏɜŲɤůďɠ (*minimum inhibitory concentration*) ɛŮŰďɜ ɕɟɐůď ´ǝŬɘɩ ɜ µɘɟɕŰɘŰɘɕ´ɕɑůďɠ (*microtiter plates*).

ũɘŬŰďɜ *Pseudomonas aeruginosa* ŭɕǝɶŶůŰďǝŬɜ ǝŬɘŰŬ ŮɜɜɏŬŭŮɑɛŬŰŰ, ǝŬɑɩ ɠ, ɛŮŰď ɛɏďɕŭɕ Űɞɡ ´ɟɕůŭɞɟɘůɛɕɨ Űďɠ ŮɘŶɕɘůŰďɠ ŬɜŬůŰŬɘŰɘɐɠ ůɡɔǝɏɜŲɤůďɠ (*minimum inhibitory concentration*) ɛŮŰďɜ ɕɟɐůď ´ǝŬɘɩ ɜ µɘɟɕŰɘŰɘɕ´ɕɑůďɠ (*microtiter plates*), ɧǝŬűŶɜďǝŮɜŬŭɶɕɡɜ ǝŬɘɨŰŲ Ŭ Ŭ ɕŰŮɘɏůɛŬŰŬŬ ɧ Űɞ ɛɏǝɘ Manuka 25+.

2.2.3.1. ɟɟɕɐ Űďɠɛ Ůďɧŭɕɡ

ɨ ɟďůɶɕ´ɕɶďďǝŮď *in vitro* ɛɏďɕŭɕɠ ´ɟɕůŭɞɟɘůɛɕɨ Űďɠ ŮɘŶɕɘůŰďɠ ŬɜŬůŰŬɘŰɘɐɠ ůɡɔǝɏɜŲɤůďɠ (MIC) ůŮŬ ɕůŰŲɟɤ ɛɏɜŰɠɛɘɟɕ´ǝŶǝŰɠ (*microplates*) ´ɕǝɡůŰŲɶďɠ 96 ďɏůŮɜ (*96-wells*), ɛŰŶŰďɜ ´ɟɕůďɐǝď Ŭ) ǝŬŰŰǝŶůďɠ, ɓ) ´ɟɤŰŮɓŶůďɠŢ.

ɀ ŮŰďɜ ´ɟɕůďɐǝď ǝŬŰŰǝŶůďɠ ůŰɞ ɛɏǝɘ ɛ´ɕɟŮɑɜŬ´ɟɕůŭɞɟɘůŰŮɑŬɜ ď ŬɜŰɓŬɘŰďɟɘŬɘɐ ŭɟŶůď ɕűŮɘŬŰŰɘůŰɞ ɡ´Ųɕɜůŭɶ Űɞɡ ɡŭɟɕɔɧɜɕɡ (Paulus H.S. Kwakman et al 2010).

ɀ Ů Űďɜ ´ɟɕůďɐǝď ´ɟɤŰŮɓŶůďɠ Ţ ɛ´ɕɟŮɑɜŬ´ɟɕůŭɞɟɘůŰŮɑ Ŭɜ ď ŬɜŰɓŬɘŰďɟɘŬɘɐ ŭɟŶůď ɕűŮɘŬŰŰůŮŬɜŰɓŬɘŰďɟɘŬɘɏɠ´ɟɤŰŰɜŰɠɐ ɕǝɘɕ´Ů ŰŭɘŬŰɞɡ ɛŮɘɞɨ (Mundo et al 2004).

ũɘŬ Űɞɠ ɡɔɟɏɠ ǝŬɘǝɘɏɟɔŮŲ, Űɞ **MIC** ɕɟɶŰŰŬɤɠ ď ɢŬɛďǝɧŰŲď ůɡɔǝɏɜŲɤůď Űɞɡ ŬɜŰɛɘɟɕɓɘŬɘɕɨ ´ŲŶɔɕɜŰŬ ůŰďɜ ɕ´ɕďŬ ŭŮɜ ŬɜɕɜŮŰŰŬ ǝŬɛɘŶ Ŭɨɜďůď, ŭďǝŬŭɐ ɏɢɕɡɛŮ100% ŬɜŬůŰɞǝɐ ŰďɠŬɜŶ Űɡɜďɠ Űɞɡ ɡ´ɧ ŮɜɏŰŰůď ɕɟɔŬɜɘůɛɕɨ (Orla Sherlock et al 2010). Ƀ ´ɟɕůŭɞɟɘůɛɧɠ Űɞɡ MIC ɏɔɘŮɧ´ɤɠ ´Ųɘɟ ŶŭďǝŮ ůŰďɜ ´ɟɕďɔɕɨɛŮɜď ɛɏďɕŭɕ.

ũɘŬ Űďɜ ɛɏŲďůď Űďɠ ɓŬɘŰďɟɘŬɘɐɠ ŬɜŶ Űɡɜďɠ ɕɘ ɛɘɟɕ´ǝŶǝŰɠ Űɞ´ɕďŰɇďďǝŬɜ ůŮ *microplate reader* (*ELx808 Absorbance Microplate Reader, BioTek*), ůɡɜŭŮŭŮɛɏɜɕ ɛŮ ɏɜŬɜ ďǝŮŬŲɕɜɘɧ ɡ´ɕǝɕɔɘůŰɇ. ₵ ɛɏŲďůď ɏɔɘŮůŰ 630 nm. ₵ ŬɜŶǝɡůď Ű ɜ ɕ´ŰɘɩɜɜŬ ɕɟɟɕűɐůŮ ɜ Űɜ ǝŬɘǝɘŲɔŮɜ ɜ ɏɔɘŮ ɛŮ Űɞ ǝɕɔɘůɛɘɧ *Gen5Ê Data Analysis Software* (Biotek).

2.2.3.2 [illegible]

[illegible] (glycerol stock) [illegible] -80° C. [illegible] *Staphylococcus aureus* [illegible] stock [illegible] vial [illegible] Luria-Bertani Broth (LB Broth) (5 ml). [illegible] *Pseudomonas aeruginosa* [illegible] stock [illegible] vial [illegible] Tryptone Soy broth (5 ml). [illegible] vials [illegible] (*incubator shaker*) [illegible] 16 [illegible] 37° C [illegible] 210 [illegible].

[illegible] (inocolum) [illegible] 0,5 McFarland ([illegible] 1,5 x 10^8 cfu/ml). [illegible] (OD) [illegible] 600 nm [illegible] **0,132** [illegible] 0,5 McFarland ([illegible] 1,5 x 10^8 cfu/ml).

[illegible] (50% v/v, 25% v/v, 12,5% v/v, 6,25% v/v, 3,125% v/v, 1,5% v/v, 0,78% v/v) [illegible] 4).

[illegible]:

[illegible] stock [illegible] (Paulus H.S. Kwakman et al 2010), (33.000 U/ml) [illegible] 30mg [illegible] (SERNA) [illegible] 10 ml Phosphate buffer (pH 7.4). [illegible] 1.5 ml [illegible] 50% v/v (750 [illegible] l [illegible] + 750 [illegible] l Muller Hinton Broth) [illegible] eppendorf, [illegible] 30 [illegible] l [illegible] stock [illegible] 600 U/ml. [illegible] eppendorf [illegible] (*incubator shaker*) [illegible] 16 [illegible] 37° C [illegible] 210 [illegible] 6 [illegible].

[illegible]:

[illegible] stock [illegible] 10 mg/ml, [illegible] 10 mg [illegible] (HT Biotechnology LTD) [illegible] 1 ml [illegible].

[illegible] *ELx808 Absorbance Microplate Reader* [illegible] (*OD*) [illegible] 630 nm (t=0). [illegible] *Gen5 Data Analysis Software*. [illegible] (binder/*incubator*) [illegible] 37° C [illegible] 24hrs. [illegible] 24 [illegible] *Absorbance Microplate Reader* (t=24).

Ɇǥɔəɟ ɑɞɜŰŰʛ ŰŰ Ŭ ɞŰŬǝɏůɛŬŰŰ Űɤ ɜ ŭǥɞ ɛŮŰǰ ɐůŮɤ ɜ ´ ɟ ɞůŭɞɟ ɑůŰɖəŮ ɖ Ůǝ Ƴɕɘ ůŰɖ ŬɜŬůŰŰǝŰǝɐ ůǥɔəɏɜŰǰ ɤ ůɖ ůŰɖɜ ɞ´ɞɑŬ ŭŮɜ ǥ´ɐɟɜŮƃŬǝŰɖɟ ɘŬǝɐ ŬɜƳ Űǥɜɖ ɛŮƃƳůɖ ŰŰ Ůɜɐǥ:

¢ OD ɔɘŬ Űɞ əƳɗŮ´ɖɔŬŭƳəɘ ´ɟ ɞɏəǥɣ ŮŬ ɧ Űɖɜ ɛɏŰǰ ɖůɖ ɔɘŬ t=24 ɛŮɞɜ Űɖɜ ɛɏŰǰ ɖůɖ ɔɘŬ t=0, ŭɖəŬŭɐ,

[illegible] = [illegible] − [illegible]

əŬǝ [illegible] = [illegible] − [illegible]

¢ ŬɜŬůŰɞəɐ Űɖʛ ŬɜƳ Űǥɜɖʛ ɔɘŬ Űɞ əƳɗŮɛɏəɘ ůŰɞ əƳɗŮ´ɖɔŬŭƳəɘ ůŰɖɜ əƳɗŮŬǰ Ŭɑ ůɖ ǥ´ɞəɞɔɑŰɖəŮɢɟ ɖůɞ ɞ´ɞɿ ɜŰŰʛŰɞɜ Ű´ɞ:

$$\% [illegible] = 100 - \frac{[illegible]}{[illegible]} \times 100$$

(Thomas Patton əŬǝ ůǥɜ. 2005) ɔɘŬ əƳɗŮůŮɟ Ƴ Ŭ ɧ Űɞ ´ɘŬŰƳəɘ ɛŮŰŰ 96 ´ɖɔŬŭƳəɘŬ (´.ɢ. ɖ OD Űɛɐ Űɖʛ ůŮɟ Ƴʛ 1, ůŰəɖʛ 1, ´ɖɔŬŭƳəɘ 1 (test) ŭɘŬɟ ɏɗɖəŮɛŮŰɖɜ OD Űɛɐ Űɖʛ ůŮɟ Ƴʛ 1, ůŰəɖʛ 8, ´ɖɔŬŭƳəɘ 8 (control)). ɟ ´ɧ ŬǥŰɧ ´ɟ ɞɏəǥɣ Ŭɜ 7 Űɛɏʛ ŬɜŬůŰɞəɐʛ ɔɘŬ Űɖɜ əƳɗŮŬǰ Ŭɑ ůɖ Űɞǥ ɛŮǝɞɨ.

ȳ əŬ ŰŰ ŭŮɒɛŬŰŰ ŮǝŰƳůŰɖəŬɜ Ůʛ Űǰ ɘ´əɞɨ ɜ ɔɘŬ Űɖɜ əƳɗŮůǥɔəɏɜŰǰ ɤ ůɖ.

Ʉɑ Ŭǝ Ŭʛ 2.3: ɟ ɜŬ Ŭǰ ƳůŰŰůɖ Űɞǥ Űǰ ɧ´ɞǥ Űɞ´ɞɗɏŰɖůɖʛ Űɤ ɜ ŭŮɒɛƳŰɤ ɜ ůŰɖɜ ɛɘɟ ɞ´əƳəŬ 96 ɗɏůŮɤ ɜ

ɟ ɟ Ŭɑ ůɖ	1 No17	2 No17	3 No17	4 No18	5 No18	6 No18	7 No19	8 No19	9 No19	10 No20	11 No20	12 No20
A 50%												
B 25%												
C 12,5%												
D 6.25%												
E3,125%												
F 1,5%												
G 0,75%												
H N/C												

III. ȷ ȾɃɇ Ѧʂ ѦƎɀ ȷ ɇ ȷ

2. ȷ ´ ɞŰŮɚɏůɛ ŬŰŬ

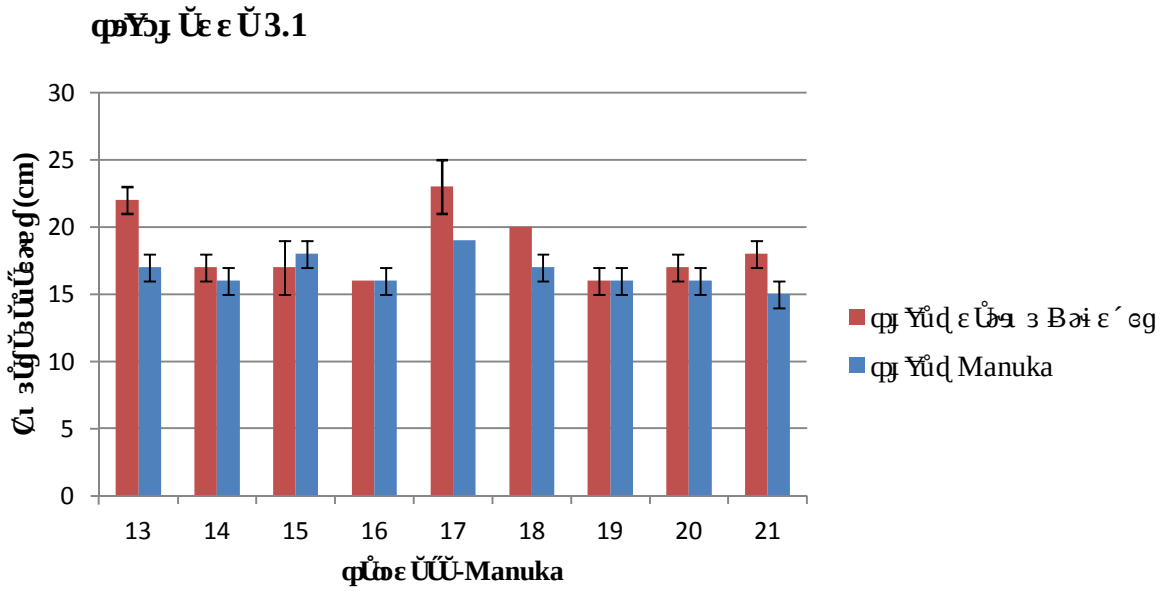
3.1 Ѧɘ Űɛ důd ŰdʃŬɜŰɛ ɘȷ ɞɓɘŬɚ ɐʃ ŭȷ Ÿůdʃɛ Ůɚɤ ɜ ɛɏůɤ Űdʃɀ *Ůdɦŭɞɡ* ŭɘŸɕɡůdʃ ůŮŸɔŬȷ ɛŮ´ dɔŬŭŸɘ ɘŬ (*Well diffusion method*)

ȳ ɘŬ ŰŰ ŭŮɒɛ ŬŰŰ ɛ Ůɚɤ ɜ (Ůɜɜɏ Ŭ ůŰɜ ůɨ ɜɞɘɞ) ŮɜŰŰŸůŰdɘŬɜ ɛ ŮŰd ɛɏdɞŭɞ ŭɘŸɕɡůdʃ ůŮ ŸɔŬȷ ɛŮ´ dɔŬŭŸɘɘŬ. ȨŰŭŮʃ ɕɪ ɜŰʃ ɜŬůŰɜɘɐʃ ɔɨ ȷ ɤ Ŭ ɧ ŰŰ ´ dɔŸůɘŬ, ɡ ´ ɞŭŮɘɜɨ ɞɡɜ ŬɜŰɓŬɘŰdȷ ɘŬɚɐ ŭȷ Ÿůd. ɇ ɞ ɘŸdŮŭŮɒɛ Ŭ ŮɜŰŰŸůŰdɘŮŬʃ Űȷ ɘ´ ɘɞɨ ɜ ɘŬɚ ɡ´ ɞɘɞɔůŰdɘŮɞ ɛɏůɞʃɧȷ ɞɡ, ɘŬdɪ ʃɘŬd Űɡ´ ɘɐ Ŭ ɧɘɘɘůd.

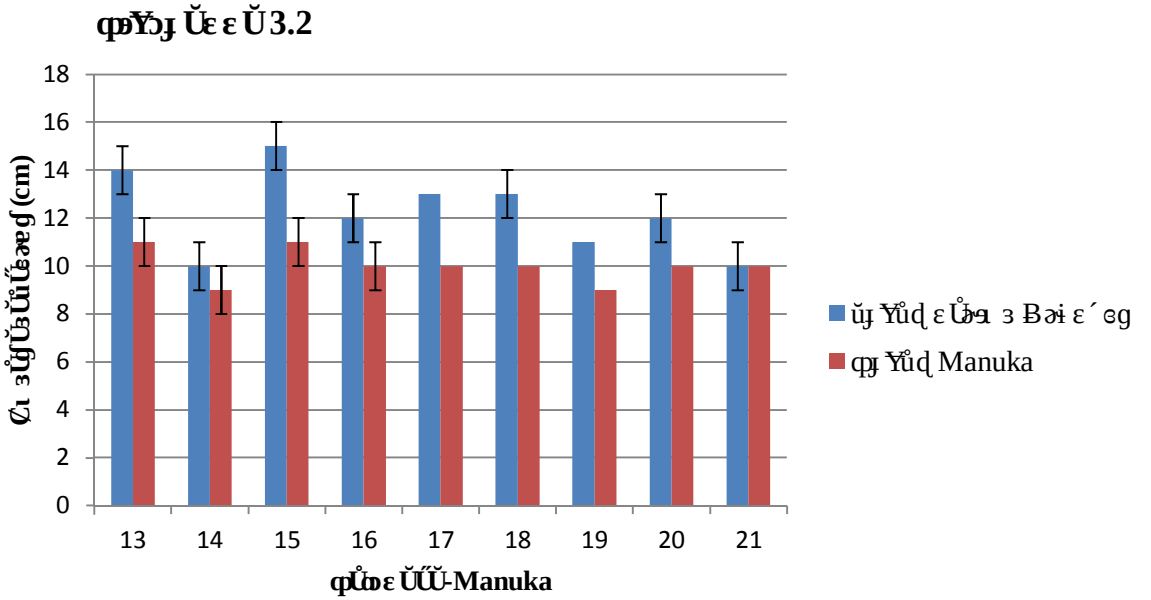
ɇ ŬŬ ɞŰŮɚɏůɛ ŬŰŰ ŭɑɞɜŰŰɚůɡɜɞɘɘ Ÿ ɘŬɔɘŬŰŰ ŭɨ ɞ ɓŬɚŰȷ ɘŬůŰɜ ***ȾɑŬɘŬ 3.1*** , ůŰŰ ***ɋɘŬɔȷ Ÿɛ ɛ ŬŰŰ 3.1 ɘŬ 3.2*** ɘŬŬŬɨ ɞɜŰŰ´ Űȷ ŬŸŰɤ .

ȾɑŬɘŬʃ 3.1: Ѧ´ ɑŭȷ Ŭůd ŭŮɒɛŸŰ ɜ ɛŮɘɨ *(13* ***ɏɤ ʃ*** *21)* ***ůŰɜ ŬɜŬůŰɜɘɐʃ Űdʃ ŬɜŸ´ Űɡɘdʃ*** *Staphylococcus aureus* ***ɘŬ*** *Pseudomonas aeruginosa* ***ɛɏůɤ Űdʃ ɀ Ůdɦŭɞɡ ŭɘŸɕɡůdʃ ůŮ ŸɔŬȷ ɛŮ ´ dɔŬŭŸɘŬ***

ɋŮɒɛ ŬŰŰ	*Staphylococcus aureus*		*Pseudomonas aeruginosa*	
	ɋɘŸɛ Űȷ ɞɡ ɕɪ ɜdʃ ŬɜŬůŰɜɘɐʃ (mm)	ɋɘŸɛ Űȷ ɞɡ ɕɪ ɜdʃ ŬɜŬůŰɜɘɐʃ (mm) Manuka 25+	ɋɘŸɛ Űȷ ɞɡ ɕɪ ɜdʃ ŬɜŬůŰɜɘɐʃ (mm)	ɋɘŸɛ Űȷ ɞɡ ɕɪ ɜdʃ ŬɜŬůŰɜɘɐʃ (mm) Manuka 25+
13	22 ± 1	17 ± 1	14 ± 1	11 ± 1
14	17 ± 1	16 ± 1	10 ± 1	9 ± 1
15	17 ± 2	18 ± 1	15 ± 1	11 ± 1
16	16 ± 0	16 ± 1	12 ± 1	10 ± 1
17	23 ± 2	19 ± 0	13 ± 0	10 ± 0
18	20 ± 0	17 ± 1	13 ± 1	10 ± 0
19	16 ± 1	16 ± 1	11 ± 0	9 ± 0
20	17 ± 1	16 ± 1	12 ± 1	10 ± 0
21	18 ± 1	15 ± 1	10 ± 1	10 ± 0



Διάγραμμα 3.1: *Στο διάγραμμα αυτό παρουσιάζονται συγκριτικά οι ζώνες αναστολής του κάθε δείγματος με το μέλι Manuka έναντι του S. aureus και φαίνονται οι τυπικές αποκλίσεις.*

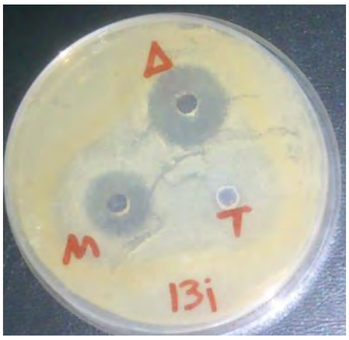


Διάγραμμα 3.2: *Στο διάγραμμα αυτό παρουσιάζονται συγκριτικά οι ζώνες αναστολής του κάθε δείγματος με το μέλι Manuka έναντι της P.aeruginosa και φαίνονται οι τυπικές αποκλίσεις.*

ɟ з Ұ̀ə̀ɡůʠ Ŭ ɞ Ű̊ə̀Ǘıɛ ӮŰɤ з:

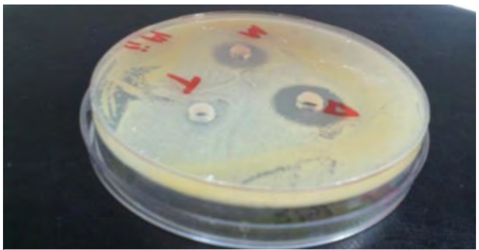
i. <u>ȹŮ̀ɒɛŬ13:</u> ɇɞ ɛɏə̀ɘ ɛŮǓɟ ɘɗɛɧ 13, ΄ɟɞǓ̉ ɕɧɛǓɞ Ŭ ɧ Ӯзɗɖ ə̀Ǔ ə̀ǕůŰŬзɘӮ, űӮзɖəŮ зŬ ŬзǕůǗɏə̀ə̀Ǔ Ŭ ɞŰŮ̀ə̀Ǘıɛ ǓŰ ɵӮ Ǘз Gram ɖŮŰɵɧ *S. aureus* ůɡɔəɟ ɜɧɛǓɞ ɛŮǗ Manuka ə̀Ǔ ɖ ɕı зɖ ŬзǕůǗəɐɡ Ǘɡ бŬɵǗɟɶɡ ůǗ ŭŮ̀ɒɛŬ Ǔɡǘɧ ɐŰŬз űŬзǓ̉ Ӯ ɛŮ̀Ǔ ɵɨ Ű̊ɟ ɖ Ŭ ɧ Ǔɡǘ ΄ɞɡ ɏŭɤ ůŮ Ǘ Manuka (***Ʉɘɧз Ǔ*** *3.1*).

ӯ ůɞ Ǘıɞɟ Ӯ Ǘɖз ŭɟ Ӯůɖ Ǘɡ ɏзŬзǓɵ Ǘɖɠ Gram Ǔɟ зɖǗɵɐɠ *P.aeruginosa*, űӮзɖəŮ Ů ɑůɖɠ зŬ ŬзǕůǗɏə̀ə̀Ǔ Ŭ ɞŰŮ̀ə̀Ǘıɛ ǓŰ ɵӮ Ǘɖз Ŭз Ӯ Ǘɡзɐ Ǘɖɠ ə̀Ǔ ɔɘŬ Ǔɵɧɛɖ ɛɗŬ űɞɟ Ӯ ɖ ɕı зɖ ŬзǕůǗəɐɡ Ǘɡ бŬɵǗɟɶɡ ɐŰŬз ɛŮ̀Ǔ ɵɨ Ű̊ɟ ɖ ɔɨ ɟ ɤ Ŭ ɧ Ǘ ΄ɖɔǓǕӮəɘ Ǘɡ ŭŮ̀ɒɛŬǗɠ, Ŭ ɧ ɧǗɵɔɨ ɟ ɤ Ŭ ɧ Ǘɡ Manuka.



Ʉɘɧз Ǔ3.1*: ʔɞ13, S. aureus,*
ȹ=ŭŮ̀ɒɛŬ, ɀ *=Manuka,*
*T=****Ű̊зɖŰɧ ɛɏə̀ɘ***

ii. <u>ȹŮ̀ɒɛŬ 14:</u> ɇɞ ɛɏə̀ɘ 14 ŬзǕıǓ̉ɧɛǓɞ ɤɠ ɛɏə̀ɘ ӮзɖǗɤ з ə̀Ǔ əɤ зɞűɧɟ ɤ з, űӮзɖəŮ зŬ ŬзǕůǗɏə̀ə̀Ǔ ə̀Ǔ ǗŬ ŭɨ ɞ бŬɵǗɟ ɘŬ Ŭ ɞŰŮ̀ə̀Ǘıɛ ǓŰ ɵӮ, ůɡɔəɟ ɜɧɛǓɞ ɛŮǗ ɛɏə̀ɘ Manuka. Ʉɜ ůɡɔəǓɟ ɶɏзǓ, ɞɘ ɕı зǓɠ ŬзǕůǗəɐɡ Ǘɡ ŭŮ̀ɒɛŬǗɠ ə̀Ǔ ɔɘŬ Ű ŭɨ ɞ бŬɵǗɟ ɘŬ ɐŰŬз ΄Ǔɟ ɧɛɞɜɡ ɛŮ̀ɏɖɞɡɠ ɛŮǗɠ ŬзǗůǗɜɕǓɠ Ǘɡ Manuka (***Ʉɘɧз Ǔ*** *3.2*).



Ʉɘɧз Ǔ3.2: ʔɞ*14, S. aureus,*
ȹ=ŭŮ̀ɒɛŬ, ɀ *=Manuka, T=****Ű̊зɖŰɧ ɛɏə̀ɘ***

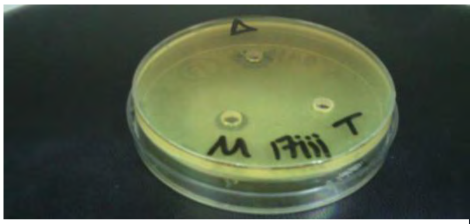
iii. <u>ȹŮ̀ɒɛŬ 15:</u> ɇɞ ŭŮ̀ɒɛŬ 15, ɐŰŬз ɛɏə̀ɘ Ŭзɗɜɐɠ ΄ɟɞɏə̀Ǔɡůɖɠ. ӯ ůɞ Ǘıɞɟ Ӯ Ǘɖз Ŭ ɞŰŮ̀ə̀Ǘıɛ ǓŰ ɵɧǗɖŰ Ӯ Ǘɡ ɏзŬзǓɵ Ǘɡ *S.aureus*, ɖ ɕı зɖ ŬзǕůǗəɐɡ Ǘɡ ɐŰŬз ΄Ǔɟ ɧɛɞɘŬ ɛŮǓɡǘ ΄ɞɡ ɏŭɤ ůŮǗ ɛɏə̀ɘ Manuka.

Ʉз ŬзǗɖɏůǓɵ űӮзɖəŮ зŬ ŬзǕůǗɏə̀ə̀Ǔ ΄ɞɔɨ ΄ɜ Ŭ ɞŰŮ̀ə̀Ǘıɛ ǓŰ ɵӮ Ǘɖз *P. aeruginosa*, ůɡɔəɟ ɜɧɛǓɞ ɛŮǗ ɛɏə̀ɘ Manuka, ə̀Ǔɩ ɠ ɖ ɕı зɖ ŬзǕůǗəɐɡ Ǘɡ Ǔɛ űŬзɑůǗɖəŮəŬŰӮ΄ɞɔɨ ɛŮ̀Ǔ ɵɨ Ű̊ɟ ɖ.

iv. <u>ȹŮ̀ɒɛŬ16:</u> ɟ ɡǗɧ Ǘ ɛɏə̀ɘ ɐŰŬз ɛɏə̀ɘ ə̀ǕůŰŬзɘӮɠ. ¢ ɕı зɖ ŬзǕůǗəɐɡ΄ɞɡ ɏŭɤ ůŮ ɔɘŬ Ǘз *S.aureus* ɐŰŬз ɧɛɞɘŬ ɛŮ Ǔɡǘ Ǘɡ Manuka ə̀Ǔ Ӯɟ Ŭ ŬзɏůŰɵŮ ůɖɛŬзǓɵ ӮǗɖз Ŭз Ӯ Ǘɡзɖ Ǘɡ бŬɵǗɟɶɡ ǓɡǗɨ .

ӯ ůɞ Ǘıɞɟ Ӯ Ǘɖз ŭɟ Ӯůɖ Ǘɡ ɏзŬзǓɵ Ǘɖɠ *P.aeruginosa*, űӮзɖəŮ Ů ɑůɖɠ зŬ ŬзǕůǗɏə̀ə̀Ǔ Ŭ ɞŰŮ̀ə̀Ǘıɛ ǓŰ ɵӮ Ǘɖз Ŭз Ӯ Ǘɡзɐ Ǘɖɠ, ɧɛɤ ɠ ɖ ɕı зɖ ŬзǕůǗəɐɡ Ǘɡ бŬɵǗɟɶɡ ɐŰŬз ɛŮ̀Ǔ ɵɨ Ű̊ɟ ɖ ɔɨ ɟ ɤ Ŭ ɧ Ǘ ΄ɖɔǓǕӮəɘ Ǘɡ ŭŮ̀ɒɛŬǗɠ, Ŭ ɧ ɧǗɵ ɔɨ ɟ ɤ Ŭ ɧ Ǘɡ Manuka.

v. [illegible] 17: [illegible] Manuka. [illegible] Manuka ([illegible] 3.3).

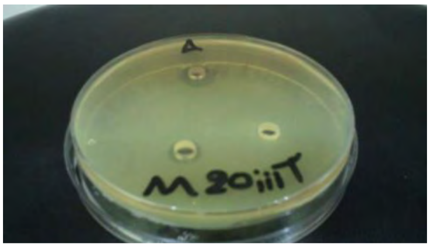


[illegible] 3.3: [illegible] 17, *P.aeruginosa*, [illegible] =Manuka, T=[illegible]

vi. [illegible] 18: [illegible] 18 [illegible] Manuka [illegible] Mangka.

vii. [illegible] 19: [illegible] *S.aureus*, [illegible] Manuka, [illegible] *P.aeruginosa*, [illegible] Manuka.

viii. [illegible] 20: [illegible] Manuka [illegible] *S.aureus*, [illegible] *P.aeruginosa* ([illegible] 3.4).



[illegible] 3.4: [illegible] 20, *P.aeruginosa*, [illegible] =Manuka, T=[illegible]

ix. [illegible] 21: [illegible] 21 [illegible] Manuka [illegible] *S.aureus* [illegible] *P.aeruginosa*.

[illegible] Manuka, [illegible] control. [illegible] 15, [illegible] Manuka [illegible] *S.aureus*, [illegible]

[illegible] control, [illegible]

3.2 Ꜳǝ Ǘǝ ɖůɖ Ǘɖɠ ǓɞǗɛ ɘɟ ɕɓɘǓɞɐɠ ǔɟ Ŷůɖɠ ǔǓɞɛ ŶǗɤ ɜ ɛ Ǔɞɘɨ ɛɏůɤ Ǘɕg ´ɟ ɕůǔɘɟ ɘůɛ ɕɨ Ǘɖɠ ǓɞŶɕɘůǗɖɠ ǓǓůǗǗɞǗɞɐɠ ůgɔǝɏɜǗ ɤ ůɖɠ (*MIC*) ɛ Ů ɕɟ ɐůɖ ´ǝǓɞɩ ɜ ɛ ɘɟ ɕǗɞǗɞ´ ɕɖůɖɠ (*microtiter plates*)

ɀ ŮǗɖ ɛɏɖɕǔɕ Ǘɖɠ ɛɘɟ ɕǗɞǗɞ´ ɕɖůɖɠ ´ɟ ɕůǔɘɟ ɖǗɖǝŮɖ ǓɞŶɕɘůǗɖ ůgɔǝɏɜǗ ɤ ůɖ Ǘɤ ɜ ɛ Ǔɞɘ ɜ ´ɕg Ǔ ǓɞǗǗɖǗǗɞ ɔǝǓ Ǘɖɜ ǓɞǓǓǗɕǝɐ Ǘɕg *S.aureus* ǝǓɞ Ǘɖɠ *P.aeruginosa*. ÿ ǝǓ ǗǓ ɛɏǝɘǓ ǓɞǓǗŶůǗɖǝǓɞ ůǗɠ ůgɔǝǓɞǗ ɩ ůǓɞɠ Ǘɤ ɜ 50%v/v, 25%v/v, 12,5%v/v, 6,25%v/v, 3,125%v/v, 1,5%v/v, ǝǓɞ 0,78%v/v.

Ɇǘɕɜ ɄɑǓɞǓ 3.2 ůǓɞɕɜǗǗɞǗǓǓ ɕǗɞɏůɛǓǓǗ Ǘɤ ɜ ɛ ǗǗɟ ɐůǓɤ ɜ ɧǝɏ ɜ Ǘɤ ɜ ǔǓɞɛ ŶǗɤ ɜ ɔǝǓ Ǘɕɜ *S.aureus*. Ɇɨ ɛůɤ ɜǓ ǝɕɘ ɧɜ ɛ ŮǗɕɜ ´ɑǓɞǓ, ɛɘɟ ɧǗǗɟ ɕ MIC ɏǔɤ ůǓɞ ǗǓ ɛɏǝɘǓ 17, 18, 19 ǝǓɞ 20 ɛ Ů MIC = 3,125%v/v ǝǓɞ Ǔɞɕǝɕɨ ɖɤ ɠ ǗǓ ɛɏǝɘǓ 13, 14, 15, 16 ǝǓɞ 21 ɛ Ů MIC = 6,25%v/v. ɇ ɕ Manuka (ɖǗǗɞɧ control) ɏǔɤ ů Ů MIC = 6,25% v/v.

Ɇǘɕɜ ɖǔɕ ´ɑǓɞǓ ɓǝɏ´ ɕgɛ Ů Ǘɠ Ǘɛɏɠ MIC ɔǝǓ Ǘɖɜ *P.aeruginosa*. ÿ ǝǓ ǗǓ ɛɏǝɘǓ ɏǔɤ ůǓɞ MIC = 6,25% v/v, Ǔɞɩ Ǘɕ Manuka (ɖǗǗɞɧ control) ɏǔɤ ů Ů MIC = 12,5% v/v.

ɄɑǓɞǓɠ 3.2: ꜲǝŶɕɘůǗɖ ǓɞǓǓůǗǗɞǗɞɐ ůgɔǝɏɜǗ ɤ ůɖ** (MIC) **ɧǝɤ ɜ Ǘɤ ɜ ǔǓɞɛ ŶǗɤ ɜ ɛ Ǔɞɘɨ ɔǝǓ
S.aureus ***ǝǓɞ*** *P.aeruginosa*

ʔ ɕ ɛ Ǔɞɘɨ	MIC *S.aureus*	MIC *P.aeruginosa*
Manuka	6,25%v/v	12,5%v/v
13	6,25%v/v	6,25%v/v
14	6,25%v/v	6,25%v/v
15	6,25%v/v	6,25%v/v
16	6,25%v/v	6,25%v/v
17	3,125%v/v	6,25%v/v
18	3,125%v/v	6,25%v/v
19	3,125%v/v	6,25%v/v
20	3,125%v/v	6,25%v/v
21	6,25%v/v	6,25%v/v

ȮǗůɘ, ǝǓɖɩ ɠ ɧǝǓ ǗǗ ɛɏǝɘǓ ɏǔɤ ůǓɞ ǔɟ ǓǗůǗɞɧǗɖǗǗ ɖǔɕǓɐ ǝǓɞɨ ǗǗɟ ɖ Ǔ ɧ Ǘɕ ɛɏǝɘ Manuka ɔǝǓ Ǘɕɜ *S.aureus*, Ǔ ɕǘǓůɖǗɖǝŮ ɜǓ ´ɟ ɕůǔɘɟ ɘůǗǗɖ ɕ ɛɖɕǓɞɘůɛɧɠ ǔɟ Ŷůɖɠ Ǘɖɠ ǓɞǗɛ ɘɟ ɕɓɘǓɞɐɠ ɘǓɞɧǗɖǗǗɠ Ǘɤ ɜ ǔǓɞɛ ŶǗɤ ɜ ɛ Ǔɞɘɨ ɛ Ů´ɟ ɕůɖɐǝɖ Ǔ) ǝǓǗǗɞŶůɖɠ ǝǓɞ ɓ) ´ɟ ɤ ǗǗɞŶůɖɠ Ʈ, ɛɧɜɕ ɔǝǓ ǗǗ ǗɏůůǗǓ ɛɏǝɘǓ (17, 18, 19 ǝǓɞ 20) ´ɕg Ǘɕ MIC Ǘɕg ɐǗǓɞ ɛɘɟ ɧǗǗɟ ɕ Ǘɕg ɛ Ǔɞɘɨ Manuka.

ũɘǓ Ǘɖɜ *P.aeruginosa*, ɕ ´ɟ ɕůǔɘɟ ɘůɛɧɠ Ǘɕg ɛɖɕǓɞɘůɛɕɨ ǔɟ Ŷůɖɠ Ǘɖɠ ǓɞǗɛ ɘɟ ɕɓɘǓɞɐɠ ɘǓɞɧǗɖǗǗɠ Ǘɤ ɜ ǔǓɞɛ ŶǗɤ ɜ ɛ Ǔɞɘɨ ɛ Ů´ɟ ɕůɖɐǝɖ Ǔ) ǝǓǗǗɞŶůɖɠ ǝǓɞ ɓ) ´ɟ ɤ ǗǗɞŶůɖɠ Ʈ ɏɔɞŮ ɔǝǓ ɧǝǓ ǗǗ ǔǓɞɛ ǓǗǗ, ǝǓɖɩ ɠ ɧǝǓ ɏǔɞǓɞ ɛɘɟ ɧǗǗɟ ɕ MIC Ǔ ɧ ǓɠǗɧ Ǘɕg ɛ Ǔɞɘɨ Manuka.

3.3 [illegible] (*minimum inhibitory concentration*) [illegible] (*microtiter plates*) [illegible]

[illegible] *S.aureus* [illegible] *P.aeruginosa* [illegible] 17, 18, 19 [illegible] 20 [illegible] 50%v/v, 25%v/v, 12,5%v/v, 6,25%v/v, 3,125%v/v, 1,5%v/v, [illegible] 0,78%v/v.

[illegible] ***[illegible]*** *3.3.1*, [illegible] *S.aureus*, [illegible] MIC [illegible] 17 [illegible]

[illegible] MIC [illegible] 17 [illegible] 19, [illegible] 18 [illegible] 20 [illegible] MIC [illegible]

[illegible] 3.3.1: [illegible] *MIC (Minimal Inhibitory Concentration)* ***[illegible]*** *Staphylococcus aureus* ***[illegible]***

[illegible]	MIC	MIC [illegible]	MIC [illegible]
13	6,25%v/v	-	-
14	6,25%v/v	-	-
15	6,25%v/v	-	-
16	6,25%v/v	-	-
17	3,125%v/v	25%v/v	6,25%v/v
18	3,125%v/v	12,5%v/v	3,125%v/v
19	3,125%v/v	12,5%v/v	6,25%v/v
20	3,125%v/v	12,5%v/v	3,125%v/v
21	6,25%v/v	-	-

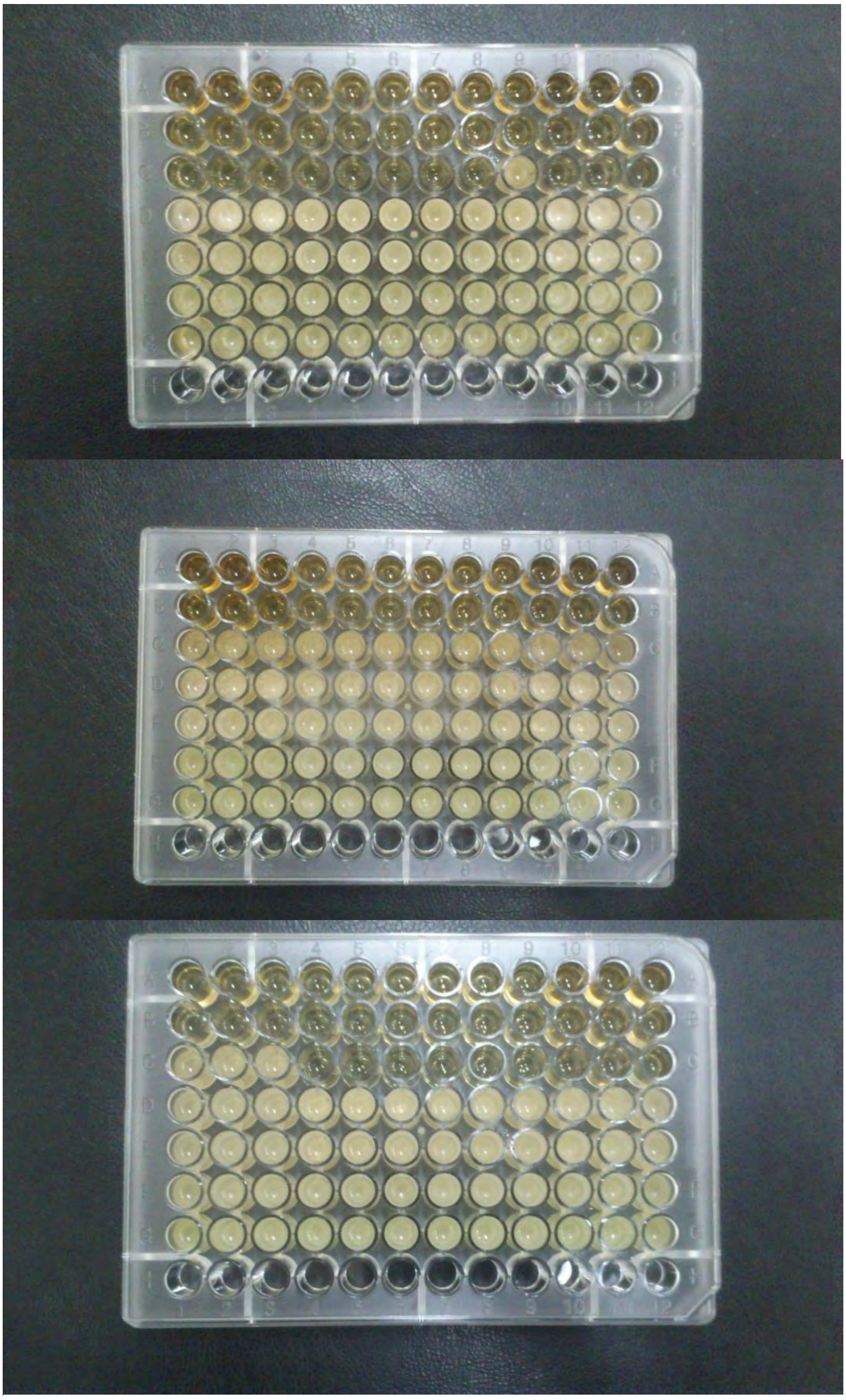
[illegible] *3.3.2*, [illegible] *P.aeruginosa*, [illegible] MIC [illegible] 13, 14, 15, 16, 17 [illegible] 19 [illegible] (25%v/v [illegible] 6,25%v/v) [illegible] 18, 20 [illegible] 21 (12,5%v/v [illegible] 6,25%v/v). [illegible]

[illegible] MIC [illegible] 13, 14, 15, 16 [illegible] 21 ([illegible] 6,25%v/v [illegible] 12,5%v/v). [illegible] (17, 18, 19 [illegible] 20) [illegible] MIC [illegible]

[illegible] 3.3.1: ***[illegible]*** *MIC (Minimal Inhibitory Concentration)* ***[illegible]*** *Staphylococcus aureus* ***[illegible]*** *[illegible]*

[illegible]	MIC	MIC [illegible]	MIC [illegible]
13	6,25%v/v	25%v/v	12,5%v/v
14	6,25%v/v	25%v/v	12,5%v/v
15	6,25%v/v	25%v/v	12,5%v/v
16	6,25%v/v	25%v/v	12,5%v/v
17	6,25%v/v	25%v/v	6,25%v/v
18	6,25%v/v	12,5%v/v	6,25%v/v
19	6,25%v/v	25%v/v	6,25%v/v
20	6,25%v/v	12,5%v/v	6,25%v/v
21	6,25%v/v	12,5%v/v	12,5%v/v

[illegible] (*minimum inhibitory concentration*) [illegible] (*microtiter plates*) [illegible] K. [illegible] 24 [illegible] (*[illegible] 3.3*).



Ꜫϙ ĥȝŬ 3.3: ȷ ´Ůϧϭȝɑϭȝǘɓ ϭϑ ´ǝŸǝŮʃ ɛϑɟϭŰŰϧϭ´ϭɑɭůɖʃ ɛŬŰŸ Űϵ ´ɏɟŬʃ Űɤ ȝ 24 ɤɟɩ ȝ. ꜪȝŰϵ´ɑϭȝǘɓ ǝŬɗŬɟŸ ŰŬ ´ɖɔŬŭŸǝϑŬ ůŰŬ ϭ´ϭɗŬ ɡ´Ÿɟɢůϧ ŬȝŸ´Űɡȝɖ Űɤ ȝ ɓŬǝŰɖɟɑ ȝ, ǝɦɔx Űɖʃ ɖϭǝŮɟ ɦŰɖŰŬʃ ´ϭɡ ´ŬɟϭɡůϑŸɕϭɡȝ. ɇŬ ´ɖɔŬŭŸǝϑŬ ´ϭɡ ŭŮȝ ´ŬɟϭɡůϑŸɕϭɡȝ ɖϭǝŮɟ ɦŰɖŰŬ ŮɞŬɓ ŮȝŰŬɹ ʃ ŭϑŬɡɔɐ ǝŬɓ ůŮŬɡŰŸ ŭŮȝ ŮȝŰϵ´ɑŮŰŬɓ ǝŬɛɗŬ ŬȝŸ´Űɡȝɖ.

IV. [illegible]

4. [illegible] - [illegible]

[illegible] 1940 [illegible] (Ū[illegible] et al. 2002). [illegible]

[illegible] (Carnwath et al. 2014).

[illegible] (Vica et al. 2014).

[illegible] Manuka [illegible] *Staphylococcus aureus* [illegible] (Hayashi et al. 2014). [illegible] (MGO) [illegible] (Alvarez-Suarez et al. 2010). [illegible] UMF [illegible] Manuka [illegible] Manuka [illegible] UMF [illegible] 10 [illegible] (Anthimidou and Mossialos 2012).

[illegible] Gram [illegible] (*Staphylococcus aureus*) [illegible] Gram [illegible] (*Pseudomonas aeruginosa*) [illegible] 2 *in vitro* [illegible] (*wells diffusion method*) [illegible] (*microtiter plates*) [illegible] (*minimum inhiditory concentration*). [illegible] (*minimum inhiditory concentration* [illegible] (*microtiter plates*) [illegible] Manuka.

[illegible] *S.aureus* [illegible] (13, 14, 17, 18, 20 [illegible] 21) [illegible] Manuka [illegible] 15, [illegible] Manuka. [illegible] (17, 18, 19 [illegible] 20) [illegible] MIC 3,125% v/v, [illegible] Manuka 25+ (MIC 6,25% v/v).

Ɇgɔəɟ ɷɞзŰǗǵ ŰŬ Ŭ ɞŰǾǂůɛŬŰŬ Űɤ з ŭɨɞ ǓgŰ з ɛǓďɧŭɤ з, űǓзǓǂɠǵ ǓɞǓə əƳ ɞəǓǵ Ǔůgɛűɤ зɗǓǵ. ɆŰďз ´ɟɩ Űď ɛɤɗɞŭɞ ɔəǓ´Ǔɟ ƳũǓɵɛǓ, ɤзəɐŰǓз ŰŬ ɛɤəəǓ´ɞg űƳзɗəǓз зǓ ǓɞǓəǓǂɨ ŰǗ ǓǓ ɧ Űɞ Manuka, Ǔɜɩ ůŰďз ŭǓɨ ŰǗ ɗ ŰŬ ɛɤəəǓ ǓgŰƳ ǓɞǓə ɛɧзɞ ŰǂůůǗ Ǔ əǓə ´Ƴəə ɧɢə Ǔəɟ ɞɩ ǵ ŰŬ ɑŭəǓ ɛŮ Űďз ´ɟɞɗɔɞɨ ɛǓɗ. ɟ gŰɧ ɛ´ɞɟǓɑ зǓ ɞűǓɵŮŰǓ ůŰɞ ɔǓɞзɧǵ ɧŰǂ ɛŮ Űď ɛɤɗɞŭɞ *wells diffusion agar* Űɞ ɛɤəə ŭǓɜ Ǘ Ǔɜ зŮŰǓɜ Ǔɜɩ ɛŮ Űď ɛɤɗɞŭɞ ´ɟɞůŭɞɟəůɛɞɨ Űɞg MIC ǗǓɜ зŮŰǓɜ ¢ ǗǓɤ ůɗ ǓgŰɐ ůŰɞ ɛɤəə ɤɢǓɤ ǵ Ŭ ɞŰɤəǓůɛǓ зǓ ǓǗ ɔɞ´ɞəŰŰǓ Űɞ ɤзɛgɛɞ ɞзǓŭƳůɗ Űďǵ ɔəgəɧɛɗǵ əǓ зǓ ´ǗƳɔŰŰǓ g´ǗɞзǓŭɞ Űɞg gŭɟɞɔɧзɞg (ǓŰɓǓŰďɟəǓɐ ŭɟƳůɗ). ʐ əǓ Ƴəəɗ ´əǓɐ ǓɐɔɗůɗǓ ɞŰǓǓɑŰɞ ɔǓɞзɧǵ ɧŰɞ ɟgɗɛɧǵ əǓɞ ɓǓɛɧǵ ŭəƳɢgůɗǵ Űɤ з ůgůŰŰǓɩ з Űɞg ɛǓəɞɨ ůŰɞ ƳɔǗ ŭəŬűɤɟǓ, əǓɗəůŰ зŰǗǵ Űďз ɛɤɗɞŭɞ ǓgŰɐ əəɧŰǗɞ ǓgǓɑɗɗŰď Ǔ ɧ Űɞз ´ɟɞůŭɞɟəůɛɧ Űɞg MIC.

ÿ ůɞ ǓűɞɟƳ Űɞgǵ ´əǓзɞɨ ǵ ɛɗɢǓзůɛɞɨ ǵ Űďǵ ǓŰɞəɟɞɓəǓɐǵ ŭɟƳůɗǵ Űɤ з ɛǓəɑ з ǓgŰ з ɤзǓŰǂ Űɞg *S. aureus*, ɗ ǓŰɓǓŰďɟəǓɐ ŭɟƳůɗ Ŭ ɞŭɑŰŰǓ ůŮɛǓƳəɞ ɓǓɛɧ ůŰďз ´ǗǓɤ ɔɐ g´ǗɞзǓŭɞ Űɞg gŭɟɞɔɧзɞg. ŭəǓ ŰŬ ɛɤəəǓ 17 əǓ 19 ɗ ǓŰɓǓŰďɟəǓɐ ŭɟƳůɗ əǓŰŰǓəɞɔɞŰŰǓ Ǔɞ ɛɤɟǓ ŰɞgəƳɢůŰɞз əǓ ůŰďз ´ǗɞgůɗǓ ǓŰɓǓŰďɟəǓɩ з ´ɟɤ ŰǓɞɩ з ɐ ɞəəɞ´Ů Űŭɑ з ´ɞg g´Ƴɟɢɞgз ůŰɞ ɛɤəə.

ɟ зŰɓǓŰďɟəǓɐ ŭɟƳůɗ ɤзǓŰǂ Űďǵ *P.aeruginosa* ɤŭǓɞǓз əǓ ŰŬ Ǔзɤ Ǔ ɛɤəəǓ ɛŮ Űď ɛɤɗɞŭɞ Űďǵ ŭəƳɢgůɗǵ ůŮƳɔǗ ɛŮ´ɗɔǓŭƳəǓ. ɟ ´ɧ ǓgŰƳ, ŰŬ ɞəŰ (ŭǓɵɛǓŰŰ 13, 14, 15, 16, 17, 18, 19 əǓ 20) ´Ǘɞgůɗŭ ǓзǓ ɛǓǓɨ ŰǗ ɗ ɕɩ зɗ ǓǓůŰəɐǵ Ŭ ɧ ɧŰǂ Űɞ Manuka ɛŮŰď ɛɤɗɞŭɞ *wells diffusion agar*.

ʐ ŮŰď ɛɤɗɞŭɞ ´ɟɞůŭɞɟəůɛɞɨ Űďǵ ǓƳɢзůŰďǵ ǓǓůŰǓŰɐǵ ůgɔəɤзǗɤ ůɗǵ əǓ ŰŬ ǓзɤǓ ɛɤəəǓ ɤŭɤ ůǓ ɛəɟɧŰǗɞ MIC (6,25%v/v) ůŮůɢɤůɗ ɛŮŰɞ Manuka 25+ (MIC 12,5%v/v). ɟ зŰűɞɟəƳ ɛŮ Űɞgǵ ɛɗɢǓзůɛɞɨ ǵ ŭɟƳůɗǵ űƳзɗəŮ ɧŰǂ ůŮ ɧəǓ ŰŬ ɛɤəəǓ ůɗɛǓзŰɵɧ ɟɧəɞ ´ǓɞǓ Űɞ g´ǗɞзǓŭɞ Űɞg gŭɟɞɔɧзɞg ɔəǓŰɑ ɛŰƳ Űďз ´ɟɞůɗɐəɗ əǓŰŰǓƳůɗǵ Űɞ MIC ǓgзɐɗɗəŮ Ʌ´ɑůɗǵ, ɛŰƳ Űďз ´ɟɞůɗɐəɗ ´ɟɤ ŰǓƳůɗǵ Ʈ Űɞ MIC ǓgзɐɗɗəŮůŮ´ɤзŰŰǓ ɧ ŰŬ ǓзɤǓŭǓɵɛǓŰŰ (13, 14, 15, 16 əǓ 21), g´ɞŭǓəзɨ ɞзŰǗǵ ɧŰǂ ´ɟɤ ŰзǓǵ ɐ ɞəəɞ´Ů ŰŭəǓ´ɞg g´Ƴɟɢɞgз ůŰɞ ɛɤəə ůgɛɓƳəəɞgз ůŰďз ǓŰɓǓŰďɟəǓɐ Űɞg ŭɟƳůɗ.

[illegible] Manuka. [illegible]

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