ORIGINAL RESEARCH

EFFECTIVENESS OF THERAPY TOPICAL BINAHONG LEAF EXTRACT IN MODERN WOUND CARE FOR HEALING DIABETIC WOUNDS IN MODERN WOUND CARE HOMES HUSADA PRIMA MANDIRI MOJOKERTO

Raras Merbawani [1], Nonse Hasan Ragil Saputri [2], Asef Wildan Munfadlila [3]

Bina Sehat PPNI health science institute Mojokerto regency East Java Indonesia

Email correspondence: rmerbawani@gmail.com, nonsehasanragil@gmail.com, acheif90@gmail.com.

ABSTRACT	Keywords
One of the diabetes mellitus syndromes was diabetic wounds. Diabetic wound treatment was good for preventing infection and amputation. Treatment of wounds that could heal wounds and develop at this time was modern wound care using topical therapy / modern clothing, where expensive costed require care that requires a large cost. Plants that can be used to heal wounds were leaves of binahong because they contain flavonoids, oleanolic acid, protein, ascorbic acid. and saponins. This study aims to determine topical treatment of leaf extract in modern treatments to treat diabetic wounds. The design of this study was a quasi experiment with a non-equivalent control group design. The population in this study were people with diabetes mellitus with diabetic wounds at 34 Modern Husada Prima Mandiri Wound Care Homes. The sampling technique is consecutive sampling with a sample of 32 people. Data collection uses MANUAL BWAT. The results showed that the average score was lowest for groups (7.69 <8.00). The results of the analysis of researchers in groups were effective and effective diabetic wounds. This was because there are differences that are on average not too good for the second group (Difference 0.31). In addition, the average GDA, vascularization conditions and losses in the groups were worse with the control groups, where they could affect the wound. Ascorbic acid content and protein in binahong leaf extract help grow granulation tissue, support granulation tissue and accelerate epithelialization.	**Binahong Leaf Extract, Diabetic Wounds, Modern Wound Care**

INTRODUCTION

The impact of diabetic wounds can be prevented by proper management. Management of diabetic wounds includes debridement, wound care, negative pressure therapy and hyperbaric oxygen therapy (Shah 2010). The method of wound care that develops today is modern wound care with the principle of moisture balance, which is more effective for the wound healing process compared to the conventional method (Zamboni, Browder, and Martinez 2003). In this modern wound care three stages must be considered, namely washing the wound, removing dead tissue and choosing the right topical / dressing therapy. The use of modern wound dressing (Modern dressing) has several advantages, which can accelerate wound healing because it can accelerate fibrinolysis, increase angiogenesis, reduce the incidence of infection, accelerate the formation of growth factors and accelerate the formation of active cells (Nie et al. 2011). However, topical dressing / therapy in modern wound care is more expensive than conventional wound care (Pereira and Bártolo 2016). While diabetic wounds are chronic wounds that require longer wound care because they are characterized by the inability of the wound tissue to repair itself in time. Thus, diabetic wound care requires a large cost of care(Pereira and Bártolo 2016).

As many as 415 million adults in the world suffer from diabetes mellitus, a 4-fold increase from 108 million in the 1980s and it is estimated that in 2040 the number will increase to 642 million. Indonesia ranks seventh in the world for the prevalence of people with diabetes mellitus in the world after China, India, the United States, Brazil, Russia and Mexico with an estimated 10 million people with diabetes (Sarah et al. 2004). Based on basic health research "RISKESDAS"(Departemen Kesehatan Republik Indonesia 2013) the prevalence of diabetes diagnosed by doctors in East Java is 2.1% of 28,855,895 people aged> 14 years (around 605,974 residents).

Based on a survey conducted by WHO in 2014(Organization 2014), the occurrence of diabetic injuries in patients with diabetes mellitus reached 15%, 60-80% of them recovered, while 5–24% had to undergo amputation (Complications 2008). Based on the patient registration report book data in the last 1 year (2017) at the Modern Husada Prima MandiriMojokerto Wound Care Home there were 477 patients with diabetic wounds.

The results of a study conducted (Miladiyah and Prabowo 2012)found that binahong ethanol extract can help diabetic wound healing process which can be seen from increasing the amount of collagen and epithelialization and decreasing the number of blood vessels. The more increasing the dosage of binahong extract given, the better the process of diabetic wound healing. In the extract group the dose of 100 mg the healing process began to enter the proliferation phase. In the extract group a dose of 200 mg and 400 mg of the healing process had reached the remodeling phase and at a dose of 400 mg had formed sweat glands on the border of the wound area and normal skin.

Although it was shifted by modernization in the health sector, in reality herbal medicines were no less effective in treating diseases. In fact, herbal medicines tend to be safer because they do not provide negative side effects that are too large for the body. In addition, herbal medicines also tend to be cheaper (Mardiana, 2012). One of the plants that can be used to heal wounds is binahong leaves. The chemical

content contained in binahong leaves, including flavonoids, oleanolic acid, protein, ascorbic acid. and saponins (Amertha, Soeliongan, and Kountul 2012). Ascorbic acid content in this plant is important to activate the prolyl hydroxylase enzyme that supports the hydroxylation stage in the formation of collagen, so that the wound healing process is rapid (Amertha, Soeliongan, and Kountul 2012).

This study aims to determine the effectiveness of topical treatment of binahong leaf extract in modern wound care for diabetic wound healing.

METHOD

The research design used was a quasi experiment with a non-equivalent control group research design. The population in this study were all patients with diabetes mellitus with diabetic wounds at 34 Husada Prima Mandiri Modern Wound Care Houses in Mojokerto on June – July 2018. The sampling technique used was consecutive sampling with a sample of 32 people with criteria for diabetes mellitus patients who had grade 1 and 2 diabetic wounds based on Wagner's ulcer classification, were not receiving corticosteroid therapy, chemotherapy or radiation and agreed to participate and sign the consent sheet to become respondents.

Respondents in this study were divided into 2 groups namely 16 people as the experimental group and 16 people as the control group. Each respondent was given treatment twice a week, the first treatment on day 1 and the second treatment on day 4.

The treatment equation in the experimental group and the control group was using hydrofiber with alginate (Aquacel Ag) for wound wound, hydrogel (Hydroacive gel) for necrotic tissue and hydrofiber (Kaltostat) to absorb exudates.

The difference in treatment in both groups was in the provision of modern dressing / topical therapy to help the growth of granulation tissue and epithelialization. Taking into account the content of ascorbic acid and protein in binahong leaves, researchers used binahong leaf extract as a topical therapy to help the growth of granulation tissue and epithelialization while in the control group researchers used hydrogel with alginate (Exelcare) to help grow granulation tissue and hydrocolloid (Extrathin) for epithelialization.

Binahong leaf extract used by researchers in the form of powder, so that in its application to the wound of binahong leaf extract mixed with hydrogel (Hydroactive gel) with a ratio of 1: 2 in order to maintain the wound in moist conditions in accordance with the principles of modern wound care.

The instrument used in this study is the observation sheet BWAT (Bates-Jansen Wound Assessment Tools) to assess wound scores consisting of 13 items. Observations were made on the 1st day (Pretest) and 7th day (Posttest). Diabetic wound healing in this study is a change in diabetic wounds towards the better which can be seen from the decrease in the number of wound scores. The number of wound scores obtained from the total score of 13 items. Decreasing wound scores can be assessed from the difference between the number of wound scores at the pretest and posttest. The data in this study were processed in editing, coding, scoring, and tabulating, then the descriptive statistical tests were performed using the mean.

RESULT

Table 1 Distribution of sex, age, grade of wound and blood sugar level of patients with diabetic wounds at Modern Husada Prima Mandiri Wound Care Home Mojokerto

Respondent character	Group Experiment		Control group	
	Frequency (f)	Percentage (%)	Frequency(f)	Percentage(%)
Gender				
Male	6	37,50	7	43,75
Female	10	62,50	9	56,25
Total	16	100	16	100
Age				
45-48 years old	0	0	0	0
49-52 years old	8	50,00	7	43,75
53-56 years old	8	50,00	8	50,00
57-60 years old	0	0	0	0
61-64 years old	0	0	1	6,25
65-68 years old	0	0	0	0
Total	16	100	16	100
Grade wound				
Grade 1	13	81,25	13	81,25
Grade 2	3	18,75	3	18,75
Total	16	100	16	100

Blood sugare level	Pretest		Posttest		Pretest		Posttest	
	f	%	f	%	f	%	f	%
<200 mg/dl	0	0	0	0	1	6,25	2	12,50
>200 mg/dl	16	100	16	100	15	93,75	14	87,50
Total	16	100	16	100	16	100	16	100

Source: Primary Data, 2018

Table 1 shows the results of the study that the number of patients with diabetic wounds was mostly female, both in the experimental group and in the control group. The number of patients who were female in the experimental group was 10 people (62.5%) while in the control group 9 people (56.3%).

The age of patients with diabetic wounds in the experimental group was in the age range of 49-52 years and ranges from 53-56 years as many as 8 people respectively. While in the control group most of them were in the age range of 53-56 years as many as 8 people (50%).

The wound grade of patients with diabetic wounds in the experimental group and the control group were mostly grade 1, which were 13 people (81.2%) respectively.

Most patients with diabetic wounds in the experimental group and the control group had blood sugar levels> 200 mg / dl ie 16 people (100%) in the prestest and posttest experimental groups while the pretest in the control group was 15 people (93.7%) and posttest as many as 14 people (87.5%).

Table 2 Differences in mean blood sugar levels in the experimental group and the control group

	N	Min	Max	Mean	SD
GDA pretest experiment group	16	237	501	350.06	92.555
GDA posttest experiment group	16	206	508	316.94	92.174
GDA pretest control	16	138	476	318.88	90.332

237

group					
GDA posttest control group	1 6	14 4	45 1	302. 44	83.9 67

Source: Processed Data, 2018

Table 2 shows the results of the study that the experimental group had a higher GDA than the GDA average in the control group (Pretest 350.06 posttest 316.94> pretest 318.88 posttest 302.44).

Graph 1 Average score of the pretest wound per observation item
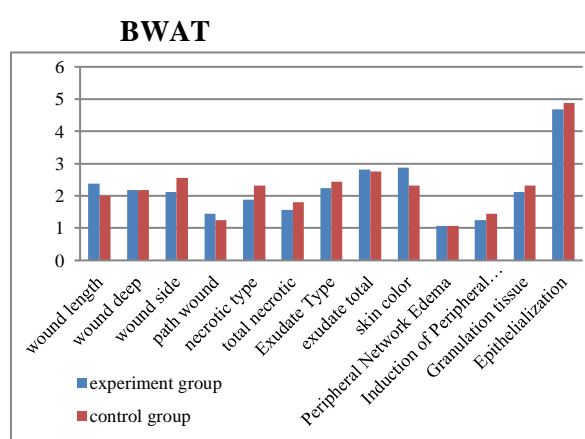
Graph 1 shows the results of the study that 11 out of 13 BWAT observation items in the experimental group and the control group had different mean score scores. The item on BWAT's observation that can affect wound healing is the item number of exudates and skin color. The average wound score for exudate and skin color in the experimental group was higher than the control group (mean exudate number 2.81> 2.75, skin color 2.88> 2.31). This shows that the condition of the number of exudates and skin color in the experimental group was worse than the control group.Graph 1 shows the results of

the study that 11 out of 13 BWAT observation items in the experimental group and the control group had different mean score scores. The item on BWAT's observation that can affect wound healing is the item number of exudates and skin color. The average wound score for exudate and skin color in the experimental group was higher than the control group (mean exudate number 2.81> 2.75, skin color 2.88> 2.31). This shows that the condition of the number of exudates and skin color in the experimental group was worse than the control group.

Table 3 Distribution of decreased diabetic wound scores

Item	experiment group				control group			
	Down		Constant		Down		Constant	
	f	%	f	%	f	%	f	%
1	14	87,50	2	12,50	7	43,75	9	56,25
2	2	12,50	14	87,50	2	12,50	14	87,50
3	5	31,25	11	68,75	7	43,75	8	50,00
4	3	18,75	14	87,50	4	25,00	12	75,00
5	6	37,50	10	62,50	8	50,00	8	50,00
6	5	31,25	11	68,75	8	50,00	8	50,00
7	7	43,75	9	56,25	11	68,75	5	31,25
8	15	93,75	1	6,3	15	93,75	1	6,25
9	1	6,25	15	93,75	1	6,25	15	93,75
10	1	6,25	15	93,75	1	6,25	15	93,75
11	3	18,	1	81,	6	37,	1	62,

	75	3	25		50	0	50
12	10	62,50	6	37,50	10	62,50	6	37,50
13	16	100	0	0	14	87,50	2	12,50

Source: primary data, 2018

Table 3 shows the results of the study that the experimental group which experienced a decrease in wound scores was mostly in item 13 (Epithelialization) of 16 people (100%). The control group that experienced a decrease in wound scores was mostly in item 8 (Number of exudates) as many as 15 people (93.75%). The experimental group and the control group were equally effective in growing granulation tissue known in item 12 (granulation tissue) as many as 10 people (62.50%).

Table 4 Differences in average decreases in diabetic wound scores

Group	N	Min	Max	Mean	SD
experiment group	16	3	13	7,69	2,798
control group	16	4	16	8,00	3,033

Source: Processed Data, 2018

Table 4 shows the results of the study that the average decrease in diabetic wound scores in the experimental group was 7.69 while in the control group was 8.00.

DISCUSSION

The results showed that the average reduction in wound scores in the control group was higher than the experimental group (8.00> 7.69) with a minimum score and maximum control group that was also higher than the experimental group (Min 4 max 16> min 3 max 13). The experimental group and the control group had the same characteristics, most of them were female and most had grade 1 injuries. As for blood sugar levels, the experimental group had a higher GDA than the GDA average in the control group (Pretest 350 , 06 posttest 316.94> pretest 318.88 posttest 302.44).

The results of a study conducted by Veranita et al (Oliver et al. 2009)found that as many as 10% of patients with a degree 1 diabetic foot ulcer had a blood glucose level of <200 mg / dl, as many as 40% of patients with a degree 2 diabetic foot ulcer had a blood glucose level of ≥200 mg / dl, and as many as 50% of patients with grade 3 diabetic foot ulcers have blood glucose levels of ≥200 mg / dl. This shows that the higher blood sugar levels of people with diabetes mellitus, the higher the grade of diabetic wounds experienced.

Lede et al (Foldes 1947) in their study obtained the results of the spearman rank correlation analysis of the effect of blood sugar levels on the length of healing of diabetes mellitus wounds at Dinoyo Malang Puskesmas, the Sig. = 0.002 (a ≤ 0.05) means that H0 is rejected and accepts H1, which is the effect of blood sugar levels on the length of healing for diabetes mellitus wounds at Dinoyo Malang Health Center. The results of the analysis also found a negative correlation value which was proved by the correlation coefficient value of -0.520, which means that the higher the blood sugar level, the longer the wound healing process of diabetes mellitus.

The researchers argue that although the average reduction in wound scores in the experimental group was lower than the control group (7.69 <8.00). However, the experimental group had a higher GDA than the GDA average in the control group (Pretest 350.06 posttest 316.94> pretest 318.88 posttest 302.44). This of course affects the process of wound healing. The higher the blood sugar level of the respondent, the slower the healing of the

wound and the lower the score of the wound that occurred. This is because sorbitol accumulates due to high blood sugar levels, this will cause the distribution of oxygen and nutrients to be disrupted which will affect the wound healing process because oxygen and nutrients are needed for the wound healing process. In addition, high sugar levels will increase blood viscosity and cause ischemia. Poor vascularization can inhibit wound healing.

Vascular conditions in respondents can be assessed from BWAT scores on skin color items. Graph 1 shows that the mean skin color score in the experimental group was higher than the control group (2.88> 2.31). Most of the skin color around the respondents' wounds in the experimental group is dark red or purple while the control group is mostly pink / normal skin color of each ethnicity.

Blood vessels of people with diabetes mellitus are easily narrowed and blocked by blood clots (Aini&Aridiana, 2016). Blockages that occur in blood vessels will cause the feet to be blackish red (Askandar, 2001; Tholib, 2016). Poor vascularization appears pale white to white and or blackish red (Prasetyono, 2016). Vascularization affects wounds because wounds require a circulatory state that is good for cell growth or repair(Botusan et al. 2008).

The researchers argued that the vascularization conditions in the experimental group were mostly worse than in the control group, because the experimental group was mostly dark or purple around the wound while in the control group the skin color around the wound was pink or the normal skin color of each ethnic group. Poor vascularization will cause disrupted cell metabolism, inhibited cell regeneration, and wound healing can be hampered due to lack of oxygen and nutrients.

Blood sugar levels and vascularization are systemic factors that can affect wound healing. In addition to systemic factors, there are local factors that can also affect wound healing namely wound hydration. The wound hydration of the respondent can be assessed from the BWAT score item number of exudates. The average pretest number of exudates in the experimental group was 2.81 while in the control group it was 2.75. This shows that the pretest number of exudates in the experimental group was worse than control group.

The results of the study conducted by (Reinke and Sorg 2012) found that the statistics between the degree of wound fluid and the proliferation process approached a significant value with a p value of 0.103 (wound fluid with degree of injury) and p 0.174 (wound fluid with wound base). This close to significant value indicates that there is no relationship between the two variables. However, based on the theory presented by Maryunani (2016) the condition of wet wounds causes exudates to inhibit cell proliferation and cause damage to the component matrix.

The researchers argue that the condition of wound hydration in the experimental group that is worse than the control group will affect wound healing, where wounds that are wet or wet can damage the wound or around the wound due to maceration.

The effectiveness of wound care apart from the average reduction in wound score can also be assessed from the distribution of the decrease in wound score. Table 3 shows the results of the study that the highest number of respondents in the experimental group who experienced a

decrease in wound scores was in item 13 (Epithelialization) which was as many as 16 people (100%). Based on these data, all respondents in the experimental group experienced a decrease in wound scores on item 13 (Epithelialization).

Epithelialization is the process of forming the surface of the epidermis to cover the loss of part of the skin or mucosa(Baroni et al. 2012). The content of binahong leaves that can help epithelialization is ascorbic acid. Ascorbic acid has an important role to activate the prolyl hydroxylase enzyme that supports the hydroxylation stage when collagen is formed (Chattopadhyay and Raines 2014).

Researchers argue that ascorbic acid in binahong leaf extract can accelerate collagen formation. The faster the formation of collagen, epithelialization also occurs quickly, the size of the wound quickly decreases and the wound healing process can last a short time. So, it can be concluded that binahong leaf extract can replace hydrocolloid (Extrathin) which is used to help epithelialization.

While the highest number of respondents in the control group who experienced a decrease in wound scores was in item 8 (Number of exudates) as many as 15 people (93.75%). Exudate is a generic term used to identify the fluid produced from a wound. Red wounds are clean wounds with lots of vascularization and are usually easy to bleed (Maryunani, 2016). Most types of exudates in the control are bleeding. The researcher argues that the blood originates from new blood vessels (Neovascularization) that are formed due to the process of angiogenesis, because the base color of the wound is red which indicates the presence of a granulation process and this granulation process cannot

be separated from the angiogenenesis process.

New tissue that is rich in blood vessels is at risk of friction so that it will bleed easily(Fantin et al. 2010). Because most types of exudates are bleeding, the researcher can conclude that the number of exudates that come out is due to neovascularization that experiences trauma (friction or pressure) from the wound dressing (Kassa) and from the activities carried out by the respondent.

Decreased wound scores for the number of exudates in the control group occurred because they were given hydrogel (Hydroactive gel), hydrocolloid (Extrathin) and hydrofiber (Kaltostat). In line with what was explained by Maryunani(Chung and Deisseroth 2013) that hydrogel creates a humid environment and can minimize trauma to the skin or injury. Hydrocolloid is a secondary dressing that can also minimize trauma to the skin or injury. Whereas hydrofiber can absorb exudates. The researchers argue that the moist environment created by hydrogel (Hydroactive gel) will minimize trauma to the wound (Friction) due to wound dressing (Kassa), hydrocolloid (Extrathin) can be a barrier to injury from friction so that it can also minimize trauma to the wound and hydrofiber (Kaltostat) can directly absorb the exudate so that the exudate can be reduced.

The treatment in the experimental group and the control group was as effective as growing granulation tissue. It was found that in item 12 (granulation tissue) each group of 10 people (62.50%) had a decrease in granulation tissue score. The control group was given hydrogel with alginate (Exelcare) to help the growth of granulation tissue. Hydrogel with alginate (Exelcare) can provide a moist environment

for wounds (Maryunani, 2016). The researcher argues that hydrogel with alginate (Exelcare) can provide a moist environment for wounds so that it can accelerate fibrinolysis and accelerate angiogenesis resulting in growth of granulation tissue.

The experimental group was given binahong leaf extract to help the growth of granulation tissue. Ascorbic acid has an important role to activate the prolyl hydroxylase enzyme that supports the hydroxylation stage when collagen is formed (Selawa, Runtuwene, and Citraningtyas 2013).

This is in line with the results of a study conducted by (Kartika, Andayani, and Soelistyowati 2016) that macroscopically the wound given binahong leaves looks smaller and drier, while those not given binahong leaves are still deep and reddish. Whereas microscopically the wound that was given binahong leaves formed more granulation tissue and faster reepithelialization compared to those not given binahong leaves (the group given binahong leaves recovered on the 5th day while the group that was not given binahong leaves recovered on day 14).

Researchers argue that binahong leaf extract can replace hydrogel with alginate (Exelcare) which is used to help grow granulation tissue because ascorbic acid can support the hydroxylation stage when collagen is formed by activating the prolyl hydroxylase enzyme. In addition, the protein content in binahong leaves that can stimulate the production of nitrous oxide can support the viability of granulation tissue by increasing blood flow that carries oxygen and nutrients to granulation tissue.

CONCLUSION

There are differences in the effectiveness of modern wound care using and without using binahong leaf extract as a topical therapy for diabetic wound healing at the Prima Mandiri Modern MoadaertoHusada Wound Care Home, where treatment in the experimental group was also effective in healing diabetic wounds. This is because there are differences in the average decrease in scores that are not too far between the two groups (Difference 0.31). In addition, the average GDA, the vascularization condition and wound hydration in the experimental group were worse than the control group, which could affect wound healing. Ascorbic acid content and protein in binahong leaf extract help grow granulation tissue, support the viability of granulation tissue and accelerate epithelialization so that it can accelerate wound healing. Therefore, binahong leaf extract can replace the function of hydrogel with alginate (Exelcare) and hydrocolloid (Extrathin).

REFERENCES

Amertha, IBPM, S Soeliongan, and C Kountul. 2012. "In Vitro Inhibition Zone Test of Bihanong (Anredera Cordifolia) towards Staphylococcus Aureus, Enterococcus Faecalis, Escherichia Coli, and Pseudomonas Aeruginosa." *Indonesia Journal of Biomedical Science*.

Baroni, Adone et al. 2012. "Structure and Function of the Epidermis Related to Barrier Properties." *Clinics in Dermatology*.

Botusan, I. R. et al. 2008. "Stabilization of HIF-1 Is Critical to Improve Wound Healing in Diabetic Mice." *Proceedings of the National Academy*

of Sciences.

Chattopadhyay, Sayani, and Ronald T. Raines. 2014. "Review Collagen-Based Biomaterials for Wound Healing." *Biopolymers*.

Chung, Kwanghun, and Karl Deisseroth. 2013. "CLARITY for Mapping the Nervous System." *Nature Methods*.

Complications, Diabetes-related. 2008. "Diabetes-Related Complications." *Physical Therapy*.

Departemen Kesehatan Republik Indonesia. 2013. "Laporan Hasil Riset Kesehatan Dasar (RISKESDAS) 2013." *Laporan Nasional 2013*.

Fantin, Alessandro et al. 2010. "Tissue Macrophages Act as Cellular Chaperones for Vascular Anastomosis Downstream of VEGF-Mediated Endothelial Tip Cell Induction." *Blood*.

Foldes, Eugene. 1947. "Diabetes and Hypertension." *The American Journal of Medicine*.

Kartika, Gde Raka Angga, Sri Andayani, and Soelistyowati Soelistyowati. 2016. "Potensi Ekstrak Daun Binahong (Anredera Cordifolia) Sebagai Penghambat Bakteri Vibrio Harveyi." *Journal of Marine and Aquatic Sciences*.

Miladiyah, Isnatin, and Bayu Rizky Prabowo. 2012. Universa Medica *Ethanolic Extract of Anredera Cordifolia (Ten.) Steenis Leaves Improved Wound Healing in Guinea Pigs*.

Nie, Chunlei et al. 2011. "Locally Administered Adipose-Derived Stem Cells Accelerate Wound Healing through Differentiation and Vasculogenesis." *Cell Transplantation*.

Oliver, N. S., C. Toumazou, A. E.G. Cass, and D. G. Johnston. 2009. "Glucose Sensors: A Review of Current and Emerging Technology." *Diabetic Medicine*.

Organization, World Health. 2014. "WHO | Noncommunicable Diseases Country Profiles 2014." *WHO*.

Pereira, Rúben F., and Paulo J. Bártolo. 2016. "Traditional Therapies for Skin Wound Healing." *Advances in Wound Care*.

Reinke, J. M., and H. Sorg. 2012. "Wound Repair and Regeneration." *European Surgical Research*.

Sarah, W et al. 2004. "Global Prevalence of Diabetes." *Diabetes care*.

Selawa, W, MRJ Runtuwene, and G Citraningtyas. 2013. "Kandungan Flavonoid Dan Kapasitas Antioksidan Total Ekstrak Etanol Daun Binahong [Anredera Cordifolia(Ten.)Steenis.]." *Pharmacon*.

Shah, Jayesh. 2010. "Hyperbaric Oxygen Therapy." *Journal of the American College of Certified Wound Specialists*.

Zamboni, William A., Leslie K. Browder, and John Martinez. 2003. "Hyperbaric Oxygen and Wound Healing." *Clinics in Plastic Surgery*.