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The Study of Synergistic Effect of Treadmill Exercise and Green Tea Extract on the Repair of Cutaneous Wound of Diabetic Mice

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Abstract

So far, a lot of research has been done on the effect of drugs and surgical procedures on the treatment of various types of ulcers, especially diabetic wounds. In his study, the effects of green tea extract (Camellia Sinesis L.) that has been widely used in different countries have been investigated and several pharmacological effects have been reported. Fifty male mice each weighing approximately 30-35 grams evaluated as adult and Healthy were divided into five groups: Healthy and Sedentary; diabetic and Sedentary; diabetic and sport; diabetic and green tea; and diabetic, sport with green tea extract. In all groups, a square shaped cut was made behind the neck of mice equal to the size of the wound cut by a surgical blade. To analyze the key roles of exercise and green tea extract in wound healing in diabetic mice, on days 14-21-14, mice were killed and after a macroscopic examination and observation of wounds, they were given a lam and a review. Microscopy has also been done. The results analyzed by ANOVA test showed that the comparison of the mean area of the control group with the training groups with treadmill exercises and the groups of enameled tea extract and showed a significant difference (P = 0.4773) and (P = 0.555), and the density of blood vessels. The epidermis was more common in these groups than in the control group and in the diabetic and dietetic group, and the combination of two factors of exercise and the use of green tea extract on the wound showed that the repair was done on day 14 and the wound healing rate 2 times faster. One of the most important factors in the healing process of wound healing is the use of medicinal herbs such as green tea extract. These medicinal herbs and also because of the presence of antioxidants, which are 100 times more effective than vitamin C and 25 times more effective than vitamin E. The chemical structure of these molecules is green tea polyphenols, which initiates the antioxidant hypothesis. EGCG (Epigaloccatin Galate) is the main component of polyphenolic green tea that contains antioxidant, anti-tumor and anti-mutagenic. EGCG is proved to be inhibitor of chymotrypsin, a factor in tumor necrosis alpha, glucose 6- Liver phosphatase, non-acceptance of transplantation in humans and lipid peroxidase. Research shows that green tea can reduce blood sugar, blood lipids, blood pressure, reduce cardiovascular disease, heart rate, and also vasodilatation. This affects the practical capacity of fibroblasts, increases the Synthesis of collagen fibers, and enhances the resistance of the wound due to increased collagen content, and since fibroblasts are responsible for creating collagen fibers. Exercise also boosts vascularity and enhances oxygenation. Therefore, it can be concluded that green tea (polyphenol catechins and EGCG) causes proliferation of fibroblasts and affects the functional capacity of fibroblasts and increases the ability to synthesize collagen fibers.

Keywords: Diabetes; Streptozotocin; Wound; Wound Healing; Green Tea Extract; Treadmill Exercise

Introduction

Today, non-communicable diseases are risk factors [1]. Diabetes mellitus is one of the most important causes of mortality in human societies, along with other factors such as high blood pressure, increased fat and smoking, and obesity as well as reduced physical activity in the occurrence and exacerbation of coronary artery disease [2,3]. Diabetes is one of the most costly diseases in many countries between the ages of 20 and 70 with complications such as blindness, organ failure and chronic renal failure. Since its definitive treatment is still inaccessible in many cases, it is

only by recognizing timely and proper care that the incidence of complications and its consequences can be significantly reduced. Sometimes beta cells degenerate without viral infections or autoimmune disorders. Type 2 diabetes mellitus is more common than type 1 and includes ninety percent of patients with diabetes mellitus. One of the effects of diabetes is the delay in the process of wound healing. Hyperglycemia can directly increase the production of reactive oxygen species (ROS). There is growing evidence that increased free radical production, due to hyperglycemia, causes oxidative stress, and therefore accelerates the onset and progression of diabetes complications [4].

Flavonoids are capable of binding ATP to enzymes and receptors. They modulate the activity of kinases directly and can have a significant effect on phosphates and act differently from kinases. High levels of flavonoids are used to prevent cancer, cardiovascular disease, and brain tumors. Green tea grows in hot weather and has a substance called cathophilic cytokine and polyphenol, all of which are antioxidants, so that their effect is 100 times more effective than vitamin C and 25 times more effective than vitamin E [5]. Wound Healing is a complicated pathophysiologic process, which is very slow in some cases, such as diabetic ulcers.

Medicinal plants and their derivatives have long been considered in the treatment of diabetes mellitus and its complications [6]. Therefore, in this study, green tea extract was used as one of the medicinal plants. The wound is also a broken tissue. Due to various factors, it has lost its connection. Nowadays, wounds and repairs have a special place of importance. Wound healing is a dynamic response to damage that is complex and regular and involves the interaction between different types of cells, building proteins, growth factors, etc. Mast cells and macrophages play an important role in wound healing.

Green tea has been introduced as an anti-inflammatory, anti-oxidative, anti-mutagenic and anticancer agent [7,8]. Studies have shown that polyphenols (flavenol and catechins) in green tea can pass through the brain duct and thus play a role in improving memory [9-11].

Green tea is anti-inflammatory due to its polyphenol combination called cathicine. Considering the mentioned properties, low side effects of herbal drugs and easy access to them, this study was conducted to determine the effect of green tea extract on the healing process of diabetic ulcers. Exercise refers to the physical activity of the body. Sports treadmills and pods are aerobic exercises that cause deeper breathing and muscle use, and cures diabetes in people [12]. Increasing blood flow and accelerating oxygen delivery accelerates the healing of wound healing [13,14]. Therefore, exercise plays an important role in wound healing. Exercise increases the oxidation of fatty acids by preventing its accumulation in muscle cells.

Epidemiological studies have shown that taking green tea prevents type 2 diabetes. There are certain serum proteins in green tea that are likely to play a role in anti-hyperglycemic effects. Reducing blood glucose also has been reported by green tea in diabetic mice with green tea [10]. Some green tea compositions have been shown to increase glucose uptake and glucose uptake by insulin in rat fat cells [15]. The lack of effect of green tea on glucose and lipid levels has also been reported [16]. Therefore, according to the different results presented by the researchers, the effect of this green tea extract and treadmill exercise was investigated in this study.

Methodology

This experimental and laboratory study was carried out at the Research Center of the Faculty of Basic Sciences of Islamic Azad University of Parand in 2013.

In this study, 50 non-infertile male mice weighing approximately 30-35 gr and over from Razi Serum Research Institute, located in Hesarak Karaj, were prepared and evaluated. The mice were divided into 5 groups of 10, based on mice are Healthy and diabetic, and motile motility is based on aerobic exercise, mice running on treadmill, using green tea extract and exercise and green tea extract.

The mice were transferred to the animal house of the Islamic Azad University of Parand and stored in clean and disinfected cages. The animal feed specialty Pellet, which was prepared from the feed stock company Trap Pars and the Razi Serum Institute was available to the animal with plenty of water. And the animals did not have any restrictions on the use of water and food and all were in the standard environmental conditions in a 12-hour dark cycle with no sound pollution. Because animal transmission causes stress and thus changes the physiological conditions in them, after the transfer of animals from the breeding and replanting of laboratory animals, serumization Razi was kept under the new conditions for two weeks in order to get adapted to their environment and the temperature of the animal's body would be balanced with the temperature of the research environment (Petan University of Parand. After two weeks, the groups were identified and each of them was categorized into 5 groups of 10.

The green tea comprises cellulose materials, resinous materials, dextrin, pectin, oily materials, starch and sugar, carbohydrates, gallic acid, oxalic acid, quercetin, proteins, fibers, minerals, caffeine or tannin as well as aromatic materials. The regular use of green tea prevents a lot of diseases such as cardiovascular diseases, cancer, skin cancer etc. and it can be positive factor to slow down the aging process.

How to Sample Blood Glucose from Mice:

Create a hole in the thinnest tail (tail end) with a needle lantern and use a glucometer and gauge tape to check the amount of glucose. In recent studies, diabetic glucose levels in mice have been reported at 250 300 dl / mg and in mice it has been declared at 180 230 dl / mg. To measure the rate of blood glucose in the diabetic mice, the researchers randomly selected one mouse and etherized it. The bile and pancreas of the mice were isolated during surgery, placed in 10% formalin and delivered to the pathologist and the final result was diabetic mice. Do not reintroduce the drug to the animal to observe the effect of the medication. After ensuring that all animals are diabetic, the next step is to start the wound. In some groups, the mouse was lost due to disability and the number of mice in the groups was reduced, so the groups were changed into 5 groups of 8 from 5 to 10 animals.

Anesthetic Method in Animals to Produce Ulcers:

After the induction of diabetes mellitus, after blood glucose was measured in the blood of the animals, and after the animals were diabetic in order to produce ulcers, the mice needed 24 hours before the fasting anesthesia.

On the day of the test, anesthetizing the ketamine Xylasein mixture was anesthetized. Anesthetic time in the mouse is 30 minutes. The dose of Ketamine Xylasein, an anesthetic drug, is 1mg / kg based on mouse weight. In more explicit terms, for every 100 grams of mice, 0.1 kg ketamine (100 λ) and 0.2 xylasein (λ 200) are used. The combination of this drug with a special insulin syringe is injected through the peritoneum.

Ketamine is an anesthetic drug that acts on its mechanism of action, such as the cycloderms. Ketamine with block of glutamate receptors in the brain thalamus prevents the transmission of pain messages to the limbic system. Xylasein (xylazine) is a supplementation of ketamine that is used as a pain reliever. It is an anesthetic and analgesic agent used in animal anesthesia.

After the peritoneal injection, the mice are placed in an empty cage, and the mice, after 20 seconds, become dizzy, rigid and have no balance in walking. After 3 minutes, the mouse is completely anesthetized with open eyes. Body temperature is normal and warm. Regular heartbeat indicates that the mouse is Healthy.

How to Get a Recovery Percentage:

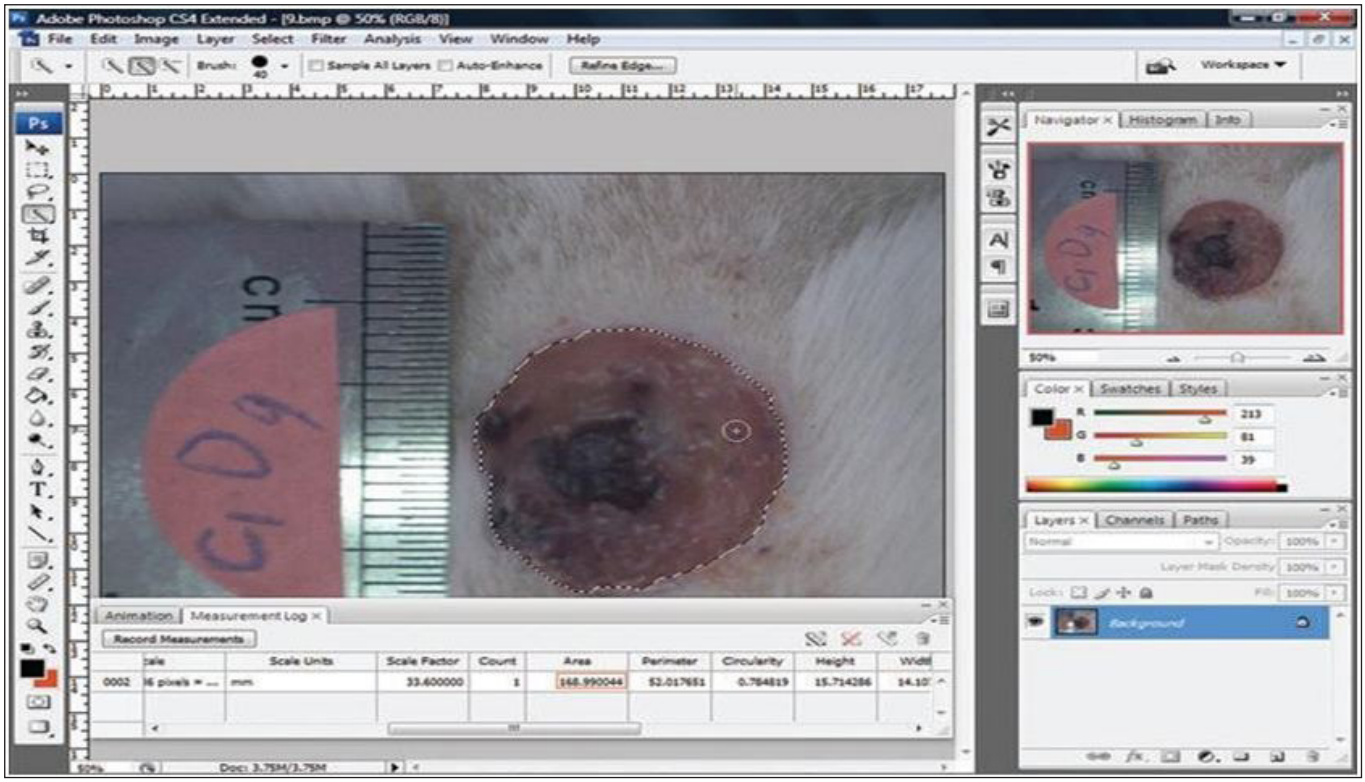
Using the following formula, the researchers get a hexadecimal:

Primary area of the wound - Wound area per day ÷ Primary area of the wound × 100

Method of Measuring the Area of the Wound

First Group:

The first group is the control group. This group was Healthy and stable and had normal blood glucose. In this group, the amount of ulcer was evaluated on certain days. Using the calisin tool, the length and width of the wound were measured and examined on days 3.7.14 .21. Therefore, the area of the wound is measured by measuring the wounds on both sides of the length and width and taking the mean. It should be noted that in the measurement with the caliper there is a great error and this measurement is based on the latest (Adobe Photoshop CS5 Extended), and the results were analyzed by a subsidy engineer and taken from the wound area and the weight of all the mice was measured by a digital balance machine and the wound area was rinsed with Saline for one day in order not to wound the infection.



The group suffered from diabetes mellitus, which was untreated and stained in the wound. In this group, the study of blood glucose and ulcer measurements with colitis and weight of the mice were performed in the same group as in the first group.

Third Group:

In this group, the animals were diabetic, and the exercise agent (running on the treadmill) was examined for wound healing. In this group, animals first became familiar with how they worked on the treadmill. Mice were rushed on a treadmill every day and in all the specific days blood glucose levels were measured and the area of the wound was examined.

Fourth Group:

In this group, the animals were diabetic, and the exercise agent (running on the treadmill) was examined for wound healing. In this group, animals first became familiar with how they worked on the treadmill. Mice were rushed on a treadmill every day and in all the specific days blood glucose levels were measured and the area of the wound was examined.

Fifth Group

This group was also diabetic and their wound healing rate was evaluated by using both treadmill exercises running on the treadmill and incision of the wound to the extract instead of green. In this group, the mice were rinsed daily for 15 minutes on a treadmill and each day was dressed with green tea extract, and finally, blood glucose levels - weight and ulcer, ulcer and ulcer area were investigated.

Sampling

To conduct histopathologic studies on days 3, 7, 14, 21 which is the representative of the phases of inflammation, proliferation, and wound closure from day three, respectively. In a randomized manner, 5 heads of mice (1 randomly on the third day, 1 on day 7, 1 on day 14, 1 on day 14 and one on day 21) and all of the groups (one control group and 4 other groups) were selected. They were killed by inhalation of chloroform in a closed environment. The specimen was prepared from the wound and Healthy skin of the adjacent skin, so that the ulcer in the middle and the two sides of the skin were Healthy and placed in the 10% formalin without washing. After the specimen was prepared, a pathology laboratory was sent to the laboratory and tissue samples were prepared on the lam.

Sampling Required Steps:

a) Steps to prepare the template for the anatomy and put samples there
b) Using Leitz microtome, transverse sections containing a Healthy skin and adjacent wound tissue with a thickness of 6 microns serially prepared.
c) Staining was performed with hematoxylin-eosin to detect inflammatory cells and fibroblasts.
d) For morphological examination in a microscopic field with a magnification of 40x and a number of vessels in 10 microscopic regions (3 regions to the left of 3 regions to the right and 4 regions in the middle of the ulcer were counted), in total, 10 parts, and from the arteries in the lower and left The field of view was discarded.

Statistical Method:

In this research, the ANOVA method was used using SPSS software, value of $p < .05$. The graphs were plotted based on the amount of fibroblasts and the area of the wound, and one hundred percent of the recovery and inflammatory cells (PMN) and the macrophage were recovered in different days.

Shot of the Wound:

It is worth mentioning that using photographs from the wound region of a specific 30+ body for all mice using a digital helix with a specific height using a metal base to insert the camera. In the first days of photography, there were obviously some errors in the picture, which, according to more accurate knowledge. The camera was used with a stronger lens and no vibration. It should be noted that shooting took place on all days from 3 to 7-14, 21.

Results

a) **Macroscopic Observations on the First Day:** Observations of the first day are the same in all groups. The ulcer of the mice is completely open, and the muscle and the underlying tissue are distinct and a large clot is located on the wound.

b) **Macroscopic and Histopathological Observations on Day Three:**

- Control group (positive) Healthy and sedentary: (Figure 2)
- Group 2: Sedentary and diabetic (negative control): (Figure 6)
- Group 3: Diabetes and exercise: (Figure 10)
- Group 4: Diabetic and Diabetes Mellitus Enriched with Green Tea Extract: (Figure 14)
- Group 5: Diabetic group with green tea with treadmill exercise: (Figure 18)
- Diabetic group and green tea extract and exercise:
- In this group, the count of fibroblasts is greater, but in comparison with the previous groups, this increase is very significant (Figure 19).

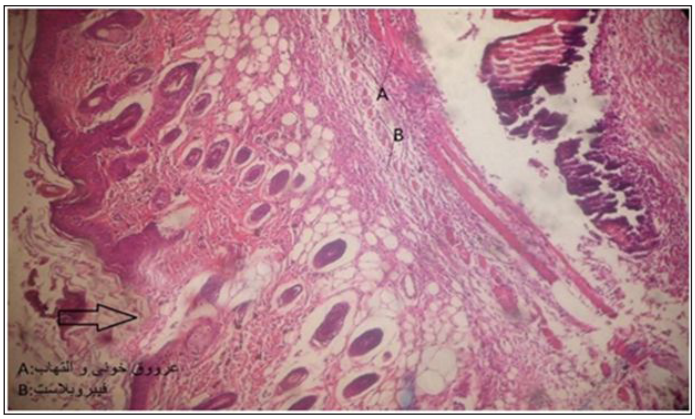
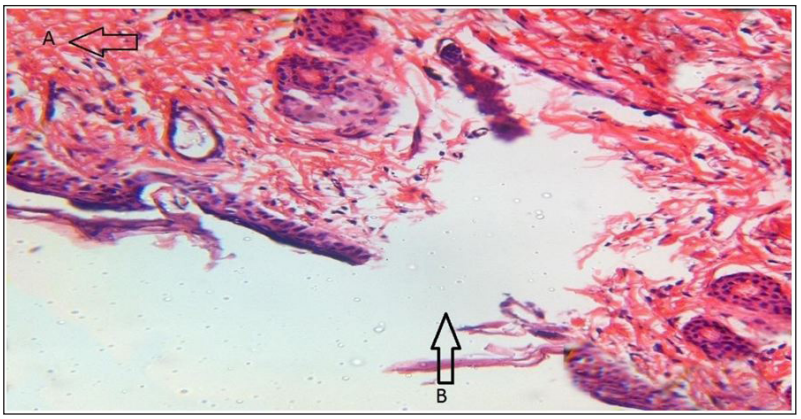
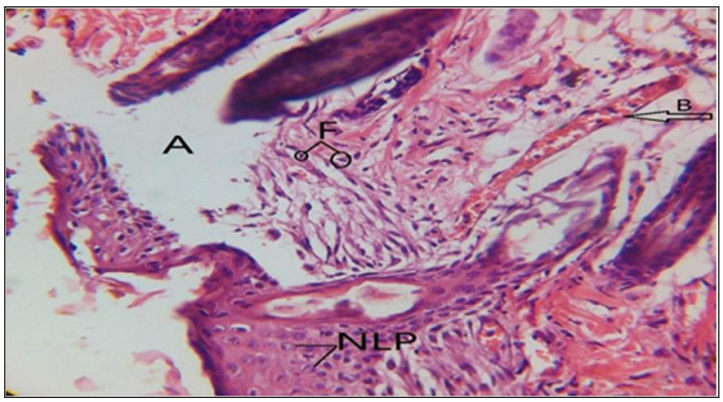


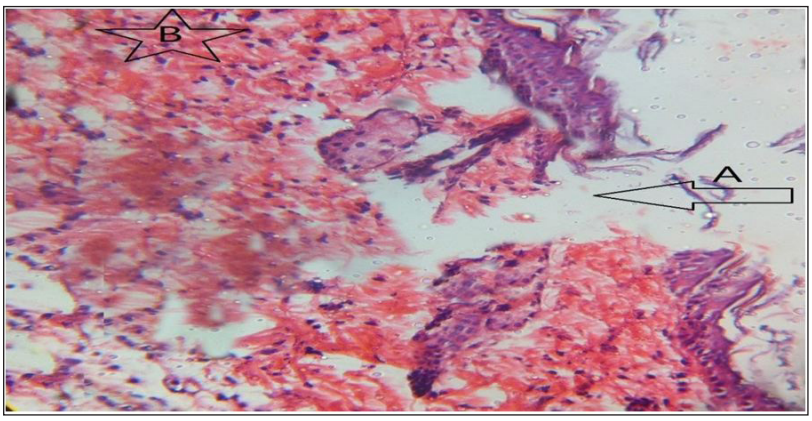
Figure 2: Day 3 post-wounding in Healthy and Sedentary Group



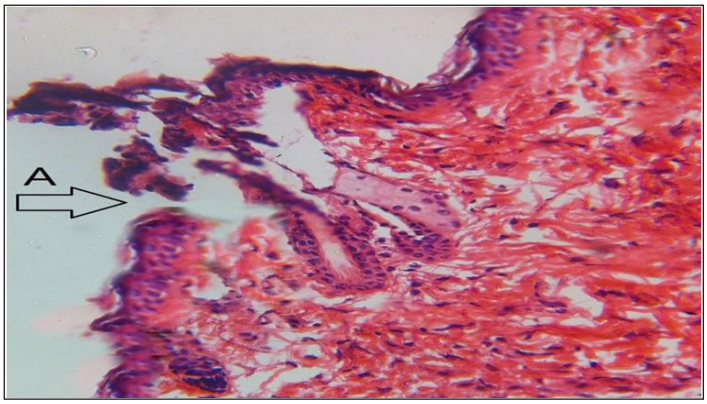
Arrow B = indicates wound area, Arrow A: Inflammation areas: neutrophil, fibroblasts, and macrophage
Figure 6: Day 3 post-wounding in Diabetic and Sedentary Group with magnification 40X



A = Wound area, B = blood vessels, F = fibroblasts, N = neutrophil
Figure 10: Day 3 post-wounding in Diabetic +Exercise group with magnification 40X



Diabetic + Tea Group
Arrow A = Wound area, star B = inflammatory area consisting of neutrophil and Macrophage cells
Figure 14: Day 3 post-wounding in Diabetic +Green Tea group with magnification 40X



Diabetic + Green Tea + Exercise Group
Figure 18: Day 3 post-wounding in Diabetic +Green Tea + Exercise group with magnification 40X (Arrow: wound area)

Arrow A = wound area, B = hair follicle, C = vascular bud
Figure 19: Day 7 post-wounding in Diabetic +Green Tea + Exercise group with magnification 40X

c) Histopathological and Macroscopic Observations on the 7th Day:

- Healthy and sedentary group: (Figure 3)
- Sedentary and diabetic (negative control): (Figure 7)
- Diabetes and exercise group: (Figure 11)
- Diabetes and tea: (Figure 15)
- Diabetic group and extract of green tea and sports: (Figure 19)

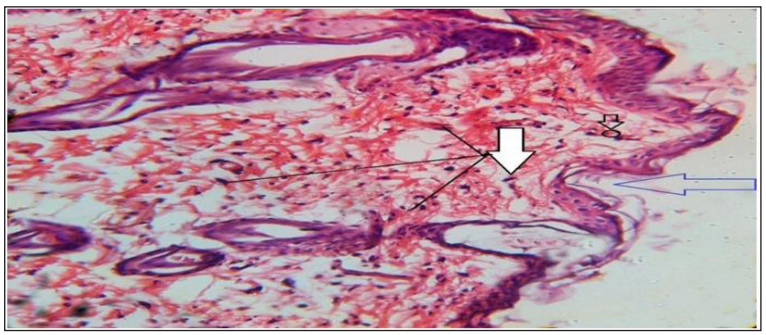


Figure 3: Day 7 post-wounding in Healthy and sedentary Group with magnification 40X (Arrow = wound area)
(White Arrow = fibroblast, circular Arrow = vascular bud, blue Arrow = wound site)

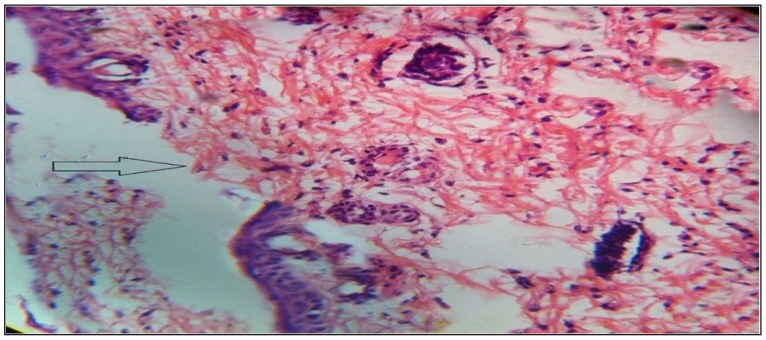


Figure 7: Day 7 post-wounding in Diabetic and Sedentary Group with magnification 40X, (Arrow = wound area)

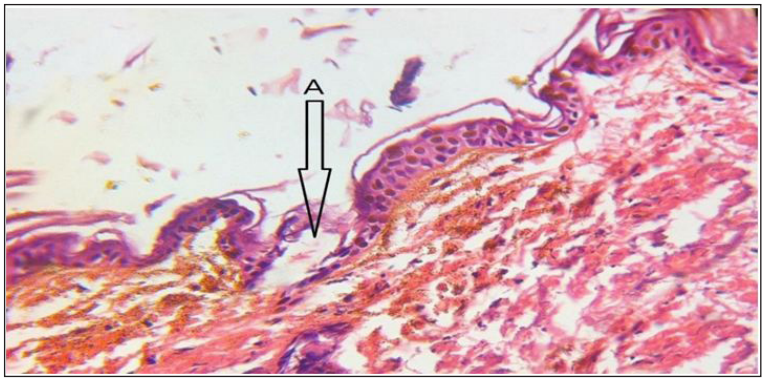
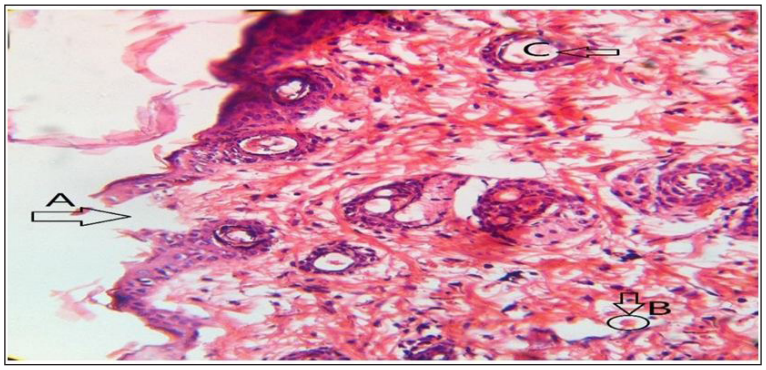


Figure 11: Day 7 post-wounding in Diabetic +Exercise group with magnification 40X (Wound healing Area: A)



Arrow A = Wound area, Arrow B = vascular bud, C = fibroblast aggregation
Figure 15: Day 7 post-wounding in Diabetic +Green Tea group with magnification 40X

d) Histopathological and Macroscopic Observations on the 14th Day:

- Healthy and sedentary group: (Figure 4)
- Sedentary and diabetic (negative control): (Figure 8)
- Diabetes and exercise group: (Figure 12)
- Diabetic group and extract of green tea: (Figure 16)
- Diabetic group and extract of green tea and sports: (Figure 20)

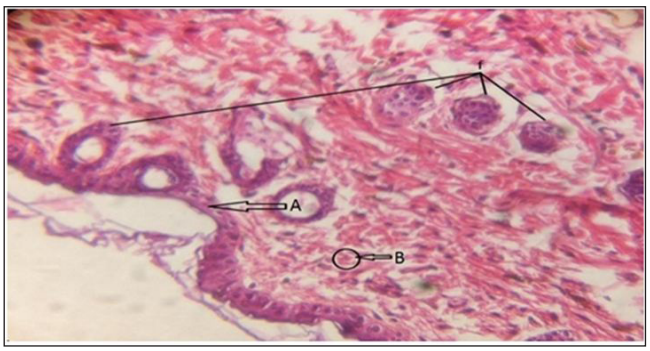
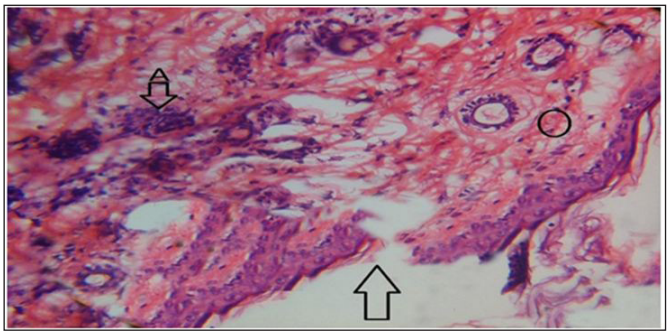
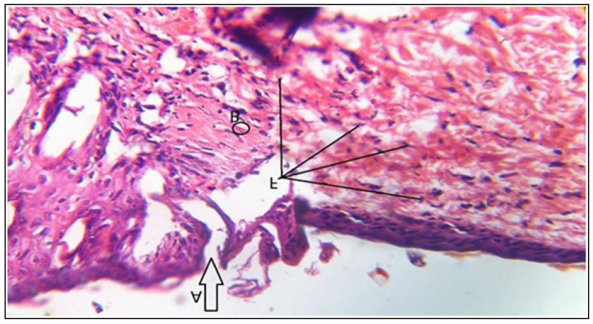


Figure 4: Day 14 post-wounding in Healthy and sedentary Group with magnification 40X (f = fibroblast, A = granule tissue formation in wound area, B = vascular bud)

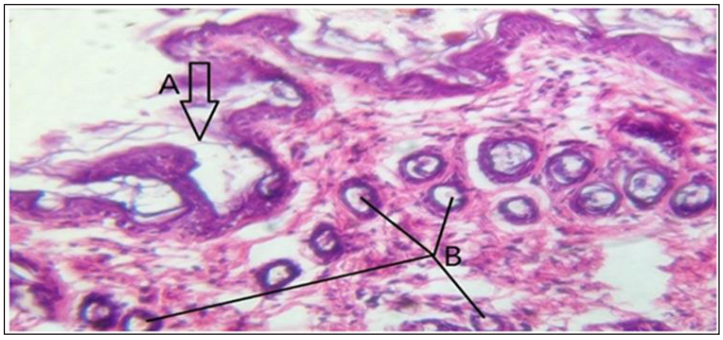


Wound area indicated by Arrow, Arrow A = fibroblast area, intracellular = vascular bud
Figure 8: Day 14 post-wounding in Diabetic and Sedentary Group with magnification 40X



A = Wound area is healing and recovering, B = Blood vessels, F = Fibroblasts
Figure 12: Day 14 post-wounding in Diabetic +Exercise group with magnification 40X

Arrow s = restored wound area, B = inflammatory area
Figure 16: Day 14 post-wounding in Diabetic +Green Tea group with magnification 40X



Arrow A = wound area, B = vascular bud
Figure 20: Day 14 post-wounding in Diabetic+Green Tea + Exercise group with magnification 40X

e) Macroscopic and Histopathological Observations of the 21st Century:

- Healthy and sedentary group: (Figure 5)
- Sedentary and diabetic (negative control): (Figure 9)
- Diabetic group with exercise: (Figure 13)
- Diabetic group with green tea extract: (Figure 17)
- Diabetic Sports and Extract of Green Tea: (Figure 21)

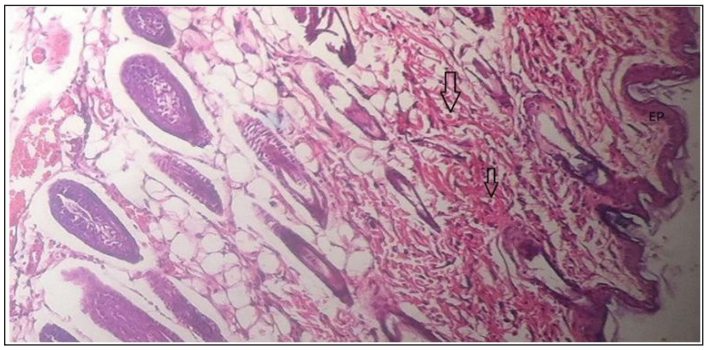
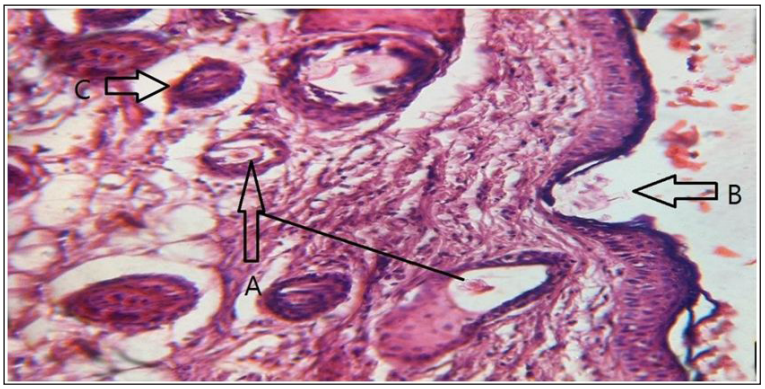


Figure 5: Day21 post-wounding in Healthy and sedentary Group with magnification 40X
(EP = Epithelium. Arrow s = Vascular Bud)



TD A = Vascular bud, Arrow s B = restored scar area, Arrow C = hair follicle Diabetic + Exercise Group
Figure 9: Day 21 post-wounding in Diabetic and Sedentary Group with magnification 40X

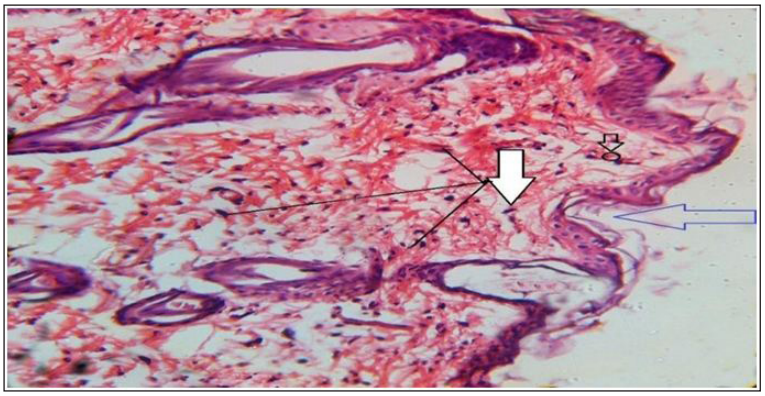
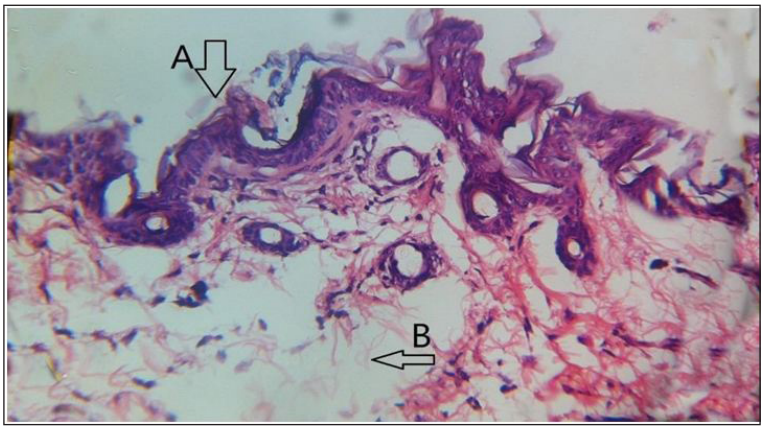
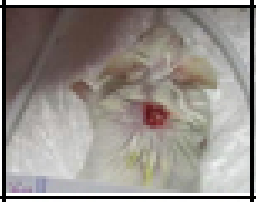
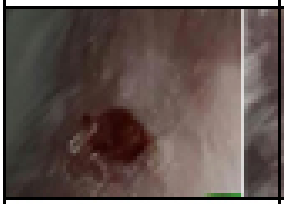
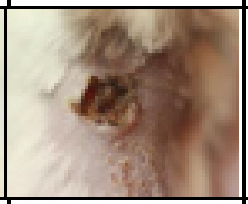
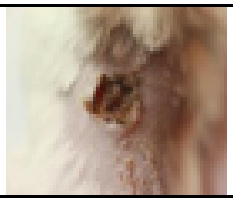
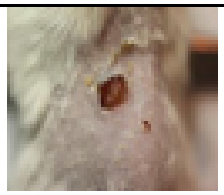
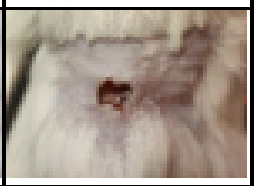
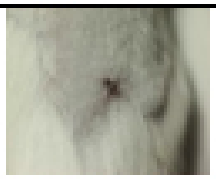


Figure 3: Day 7 post-wounding in Healthy and sedentary Group with magnification 40X (Arrow = wound area) (White Arrow = fibroblast, circular Arrow = vascular bud, blue Arrow = wound site)



Arrow A = Wound Healing. Arrow B = Collagenization
Figure 17: Day 21 post-wounding in Diabetic +Green Tea group with magnification 40X

Arrow = wound area is completely repaired
Figure 21: Day 21 post-wounding in Diabetic +Green Tea + Exercise group with magnification 40X

Healthy and Sedentary on the first Day	Diabetes and sedentary on the first day	Diabetes and exercise on the first day	Diabetes and tea on the first day	Diabetes and tea and exercise on the first day
				
Healthy and sedentary on the third day	Diabetes and sedentary on the third day	Diabetes and exercise on the third day	Diabetes and tea on the third day	Diabetes and tea and exercise on the third day
				
Healthy and sedentary on the seventh day	Diabetes and sedentary on the seventh day	Diabetes and exercise on the seventh day	Diabetes and tea on the seventh day	Diabetes and tea and exercise on the seventh day
				
Healthy and sedentary on the 14th day	Diabetes and sedentary on the 14th day	Diabetes and exercise on the 14th day	Diabetes and tea on the 14th day	Diabetes and tea and exercise on the 14th day
				
Healthy and sedentary on the 21st day	Diabetes and sedentary on the21st day	Diabetes and exercise on the 21st day	Diabetes and Tea on the 21st day	Diabetes and tea and Exercise on the 21st day

Day 3 Post-Wounding: Due to the fact that the mean area of the wound was not meaningful in the two groups (Healthy and sedentary) and (diabetic and sedentary) the rest Groups are also not considered.

Day 7 Post-Wounding: Comparing two groups (Healthy and sedentary) with (diabetic and sedentary group), there was a significant difference ($p = 0.0$) and +++.

In this day, the exercise group and diabetes also had a significant reduction ($p = 0.003$) and p * and * indicate the presence of two stars.

In the tea group, a significant decrease was observed (p = 0.039) and p (p = 0.039). In the tea group with exercise, there is a significant decrease (p = 0) and (***).

Day 14 Post-Wounding: Comparing two groups (Healthy and sedentary) and (diabetic and sedentary), there is a significant difference, so (0) = p

And +++ are in the exercise group, which has a significant decrease (p = 0.008) and **.
In the tea group, there is a significant decrease (= 016/0) and * in the tea group. There is a significant difference in the diabetic group with exercise and tea with (0) = p and ***.

Day 21 Post-Wounding: After comparison, there is a significant difference between two groups (Healthy and sedentary) and (diabetic and sedentary) with p = 0. 0 and p <0.05 respectively. In the exercise group, p = 0 and p < Is it in the tea group, p = 0 and p = 0, representing a significant decrease.

Also, in the tea group with exercise, p = 0 and p = 0, which shows a significant difference, but it is not possible to determine which factor (exercise or tea) is effective.

Average area of the wound on certain days post-wounding				
Experimental groups	Day 3	Day 7	Day 14	Day 15
Healthy + sedentary	1.25±0.27	0.83±0.34	0.50±0.08	0.141±0.047
Diabetic + sedentary	1.29±0.14	0.96±0.049	0.73±0.1	0.23±0.049
Diabetes + Exercise	1.148±0.98	0.90±0.022	0.58±0.1	0.588±0.033
Diabetes + Tea	1.06±0.29	0.090±0.032	0.59±0.05	0.032±0.0183
Diabetes + Tea + Exercise	1.027±0.90	0.86±0.026	0.36±0.08	0.0075±0.007

Table 1: Average area of the wound in the specified days

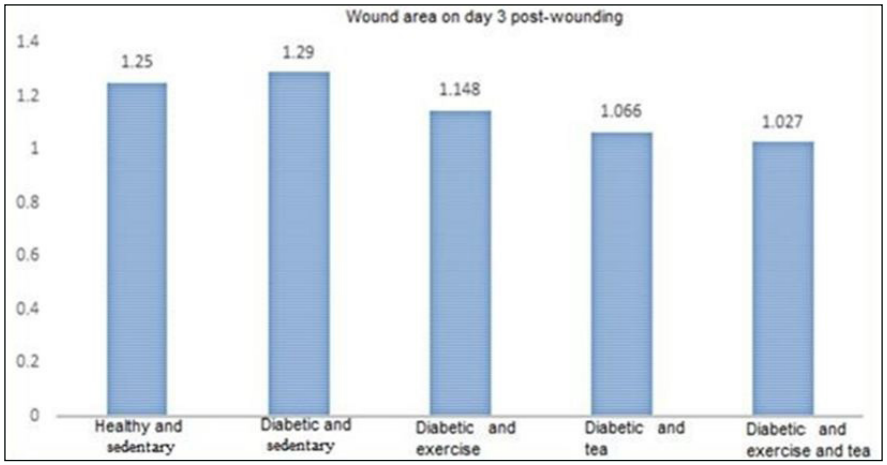


Diagram 1: The area of the wound on the third day

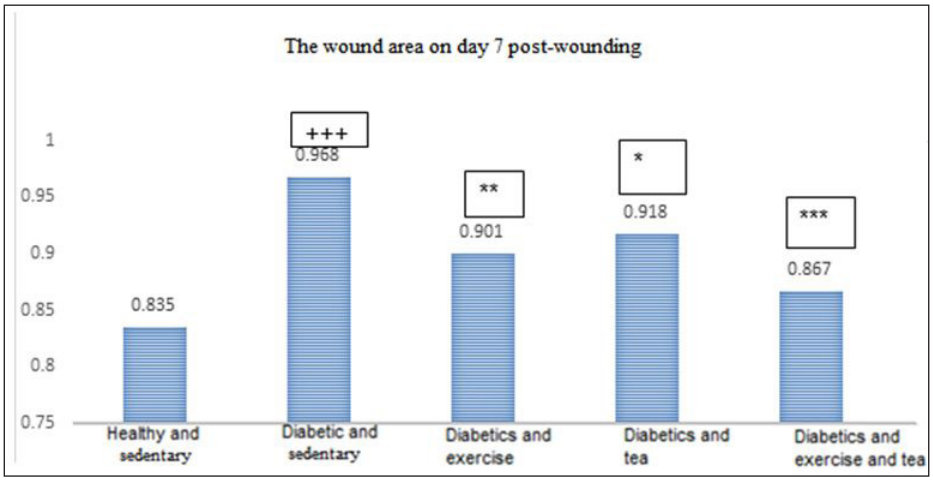


Diagram 2: The area of the wound on the seventh day

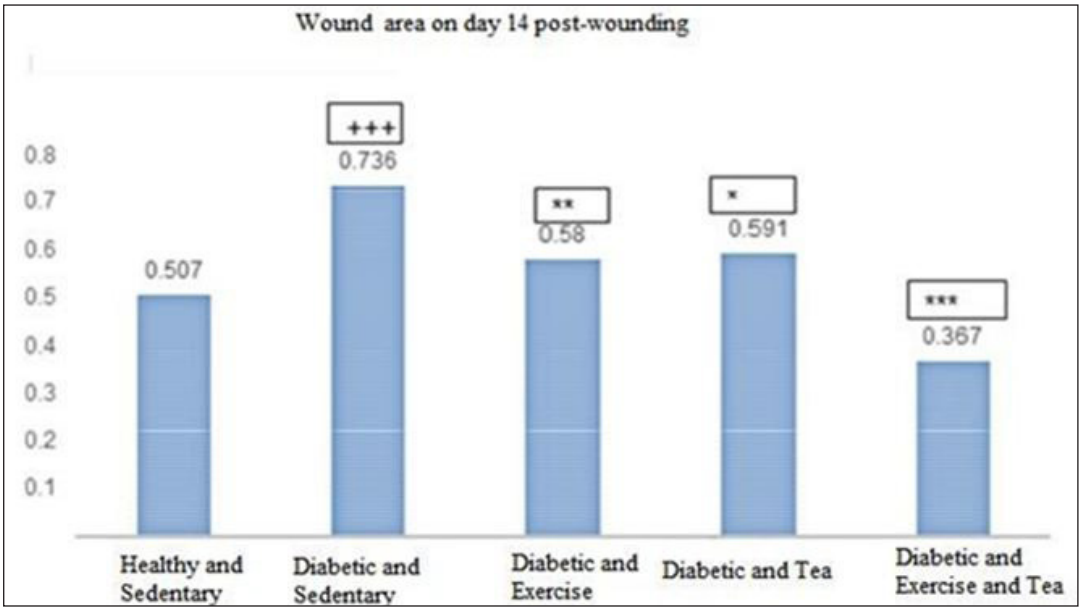


Diagram 3: The area of the wound on the fourteenth day

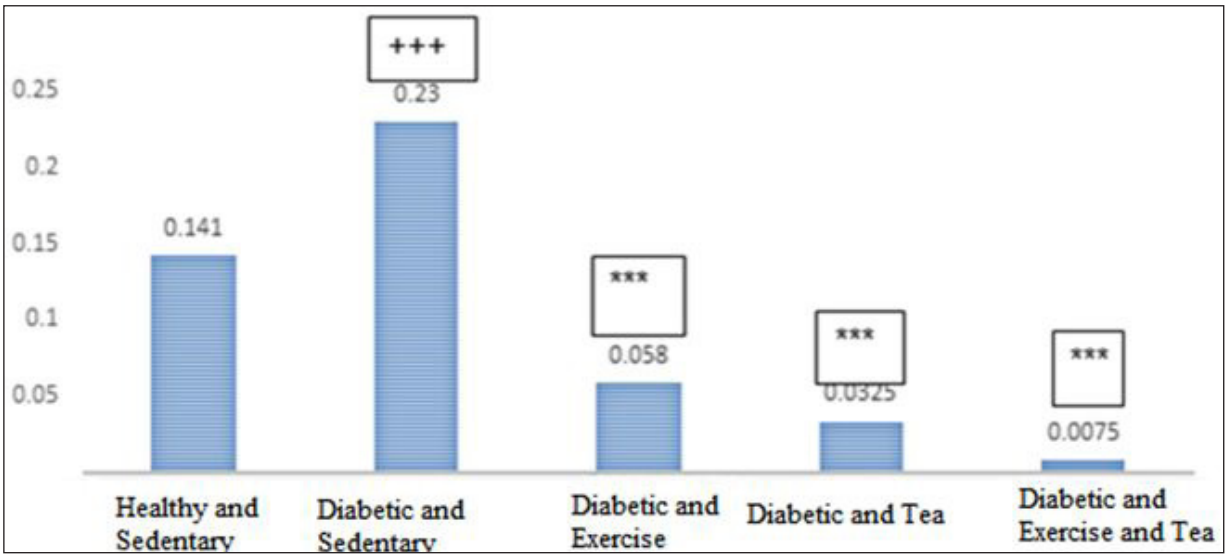


Diagram 4: The area of the wound on the21th day

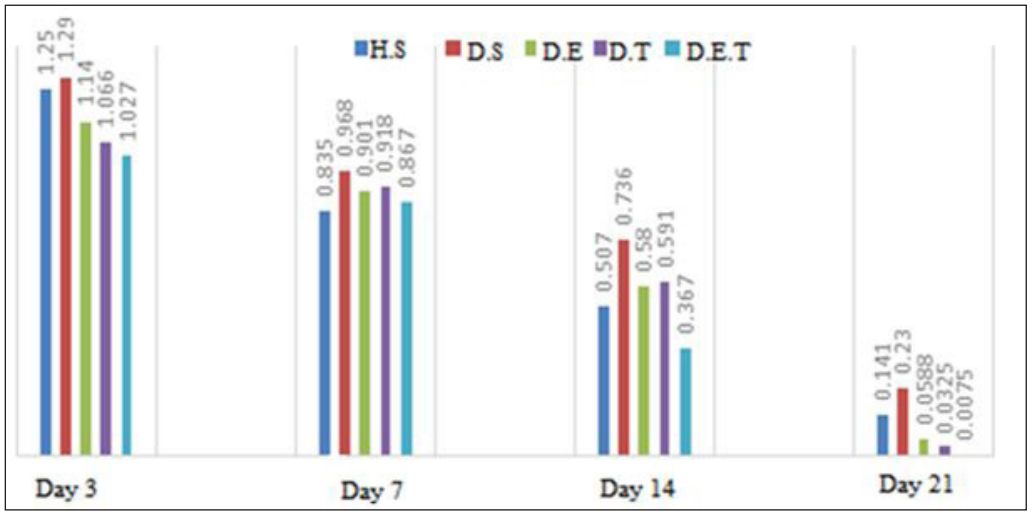


Diagram 5: The area of the wound on different days

Experience 2:

- **Third Day:** Due to the non-meaningfulness of the mean, the mean for improvement in the two groups (Healthy and sedentary) and (diabetic and sedentary) is discarded from the rest of the groups.
- **Seventh Day:** Due to the non-meaningfulness of the mean, the mean for improvement in the two groups (Healthy and sedentary) and (diabetic and sedentary) is discarded from the rest of the groups.
- **14th day:** Due to the meaningfulness of the two groups (Healthy and sedentary) and (diabetic and sedentary), which are 0 = p and +++, the other groups are examined. In the exercise group, p = 0.001 and p Has a significant increase. The tea group also had a significant increase with p = 0.028 and *. In the teas group with exercise, p = 0 and p = 0, indicating a significant increase.
- **21st day:** Due to the significance of the two groups (Healthy and sedentary) and (diabetic and sedentary), which is obtained by P = 0.001 and +++

Wound healing rate in certain days post-wounding				
Day 21	Day 14	Day 7	Day 3	Test groups
85.87 ± 4.76	48 ± 6.82	16.50 ± 3.46	25.37 ± 2.72	Healthy + Sedentary
77.75 ± 4.95	26.37 ± 10.14	3.62 ± 4.56	29 ± 14.93	Diabetic + sedentary
93.87 ± 3.3	44.5 ± 10.91	18.62 ± 25.24	15.87 ± 8.90	Diabetes + Exercise
96.75 ± 1.83	39.62 ± 4.03	8.12 ± 3.27	3.87 ± 6.97	Diabetes + tea
99.25 ± 0.70	63.25 ± 8.77	13.25 ± 2.60	7.25 ± 5.47	Diabetes + tea + Exercise

Table 2: Average percentage of wound healing on the specified days

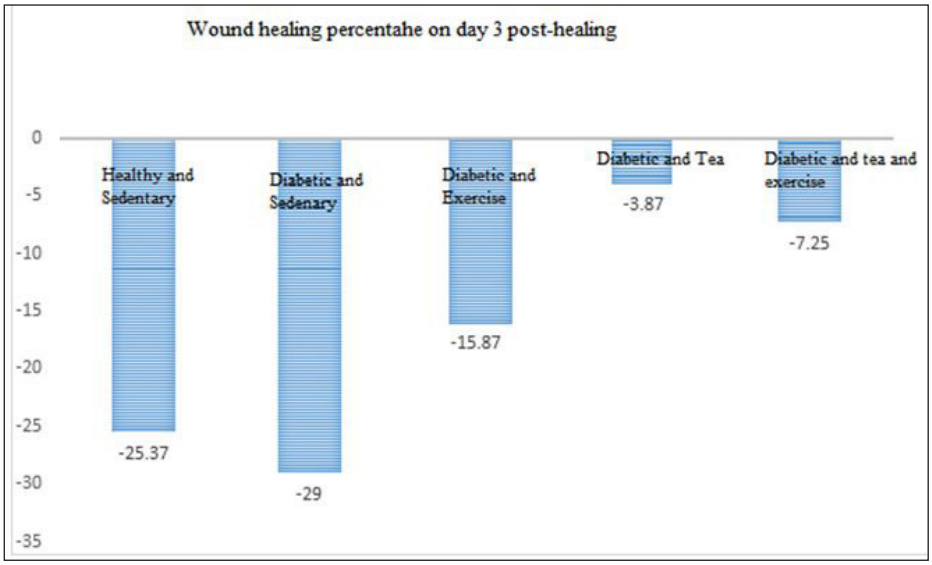


Diagram 6: Wound healing percentage on3 post-healing

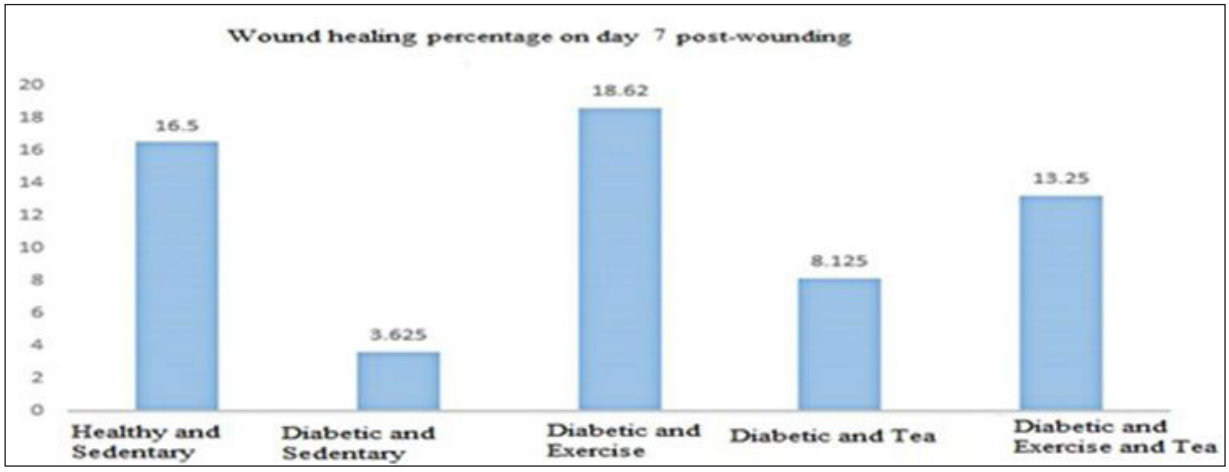
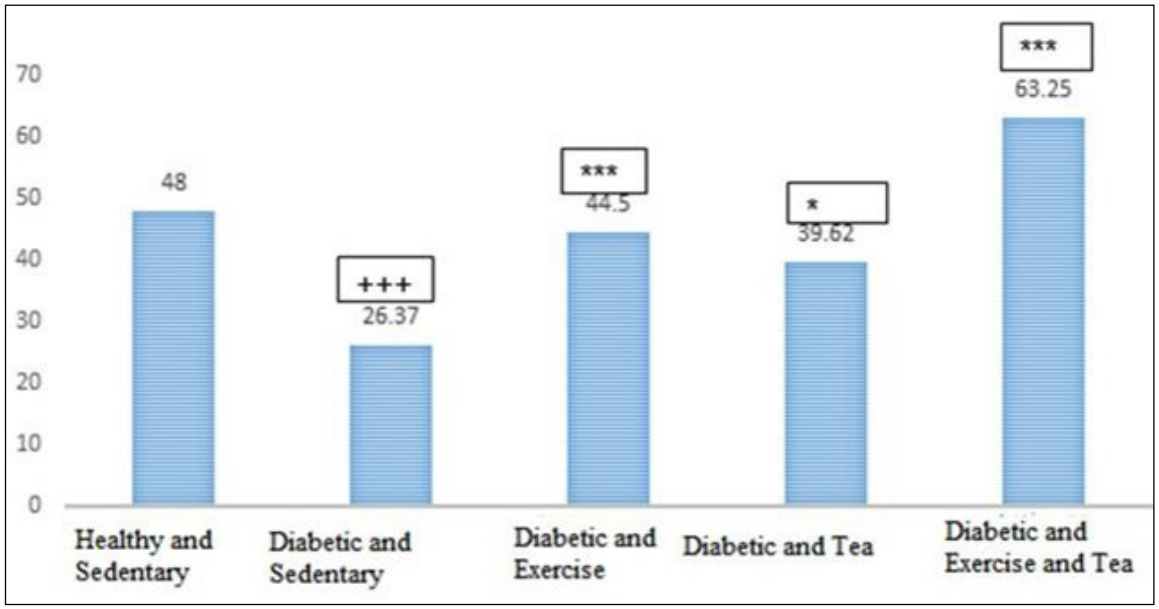
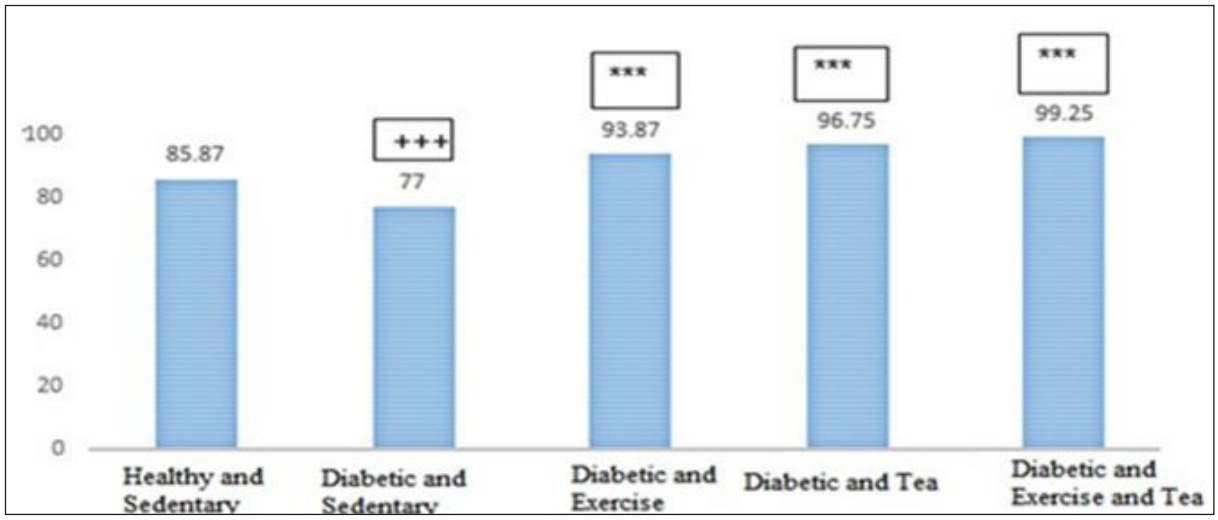


Diagram 7: Wound healing percentage on7 post-healing



(+++) and (*** p <.001) and (* p <.05)
Diagram 8: Wound healing percentage on14 post-healing



(+++) and (***) p <.001
Diagram 9: Wound healing percentage on21 post-healing

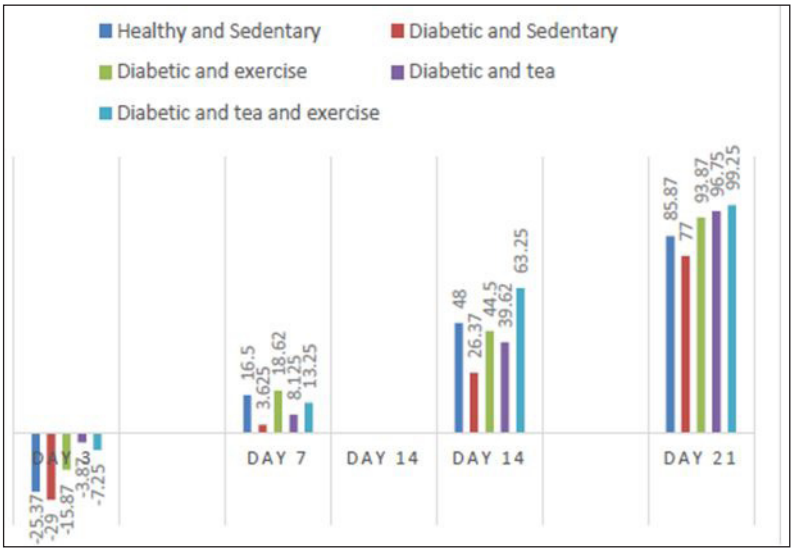


Diagram 10: Healing percentage on different days post-wounding

Experience 3:

- **Day 3 Post-Wounding:** By comparing the mean number of fibroblasts between two groups (Healthy and sedentary) and (diabetic and sedentary), no significant difference was observed, therefore, other groups were excluded.
- **Day 7 Post-Wounding:** Comparing the mean number of fibroblasts between two groups (Healthy and sedentary) and (diabetic and sedentary), there is a significant difference of p = 0.027 and so the other groups are as follows: in the exercise group, p = 0.002 and ** and there was a significant increase in the control group. In the tea group, it was also p = 0/7 and p = 0, respectively, and showed a significant increase compared to the control group. In the tea group, P = 0/0, and the increase in meaning you are seen with the control group.
- **Day 14 Post-Wounding:** Comparing the number of fibroblasts between two groups (Healthy and sedentary) and (diabetic and sedentary), there was a significant difference between the two groups (p = 0.022 and p = 0.02). On this day, exercise group with p Shows a significant decrease compared to the control group in the tea group (p = 0.007).
- In the same group, exercise with tea was also found to be 2 p <0.001 and ** significant decrease was observed in the control group, indicating that the reconstitution phase of collagen synthesis was started faster in the treated group.
- **Day 21 Day Post-Wounding:** After comparing the mean number of fibroblasts in both groups (Healthy and sedentary) and (diabetic and sedentary), no significant difference was observed, so other groups were prevented.

Average fibroblasts on different days post-wounding				
Test groups	**Day 3**	**Day 7**	**Day 14**	**Day 21**
Healthy + Sedentary	9± 0.01	25.5±3.97	22.20±2.09	19.20 ±9.23
Diabetic + sedentary	11.5±2.79	21.10±1.85	29.30±9.40	18±2.66
Diabetes + Exercise	12.60±2.45	26.90±3.84	22.30±3.49	18.10 ±2.37
Diabetes + tea	14.20±3.61	26.20±3.25	21.20±2.39	17.60±1.42
Diabetes + tea + Exercise	11.72±3.20	27.50±2.46	20.10. ±3.92	16.50±2.31

Table 3: Average fibroblasts on different days post-wounding

Average cell (PMN) on different days post-wounding				
Test groups	**The average of the 3 day**	**The average of the 7 day**	**The average of the 14 day**	**The average of the 21 day**
Healthy + Sedentary	9.40 ± 1.34	8.60 ± 1.71	2.40 ± 1.71	2.80 ± 1.75
Diabetic + sedentary	20.70 ± 2.71	12.70 ± 2.58	3.80 ± 1.47	5.60 ± 1.64
Diabetes + Exercise	15.70 ± 4.19	9.20 ± 2.78	3.20 ± 2.20	3.30 ± 1.15
Diabetes + tea	7.40 ± 1.95	4.50 ± 2.01	2.40 ± 1.83	2.40 ± 2.41
Diabetes + tea + Exercise	5.50± 3.50	2.40 ± 2.02	3 ± 2.21	2.1 ± 1.66

Table 4: Average cell (PMN) on different days Post-wounding

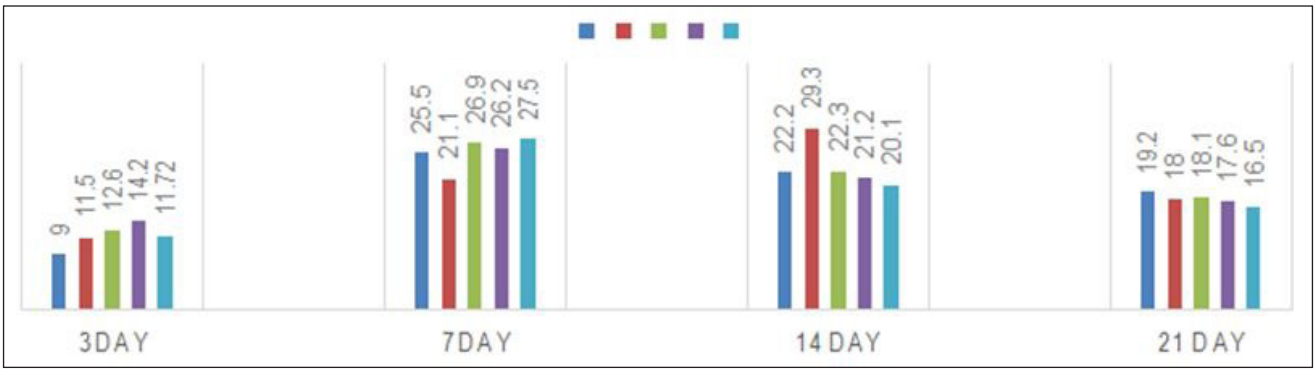


Diagram 11: Average fibroblast on different days post-wounding

Experience 4:

- **Day 3 Post-Wounding:** Comparing the mean of inflammatory cells (PMN) in both groups (Healthy and sedentary) and (diabetic and sedentary), there is a significant difference between the two groups, and p = 0 and P ++ +. In the exercise group, p = 0/00 = There was a significant decrease in the control group. In the tea group, p = 0 and p <0.05 respectively, which again showed a significant decrease with the control group. And in the tea group, with exercise, p = 0 and p <0.05 respectively, with a meaningful decrease with the control group.

- **Day 7 Post-Wounding:** Comparing the mean of PMN inflammatory cells in both groups (Healthy and sedentary) and (diabetic and non-diabetic), a significant difference was seen between P and P = 0.055 and the other groups were as follows: In the exercise group, P * There is a significant reduction in the control group. In the tea group, with P = 0 and ***, there was a significant decrease in the control group. Also, in the exercise group with tea, P = 0 and P = 0, there was a significant decrease with the control group. This suggests that the inflammation in this group has slowly decreased and the stage of reproduction has begun.
- **Day 14 Post-Wounding:** Comparing the mean of PMN inflammatory cells in both groups (Healthy and sedentary) and (diabetic and sedentary), no significant difference was observed, and other groups were discarded.
- **Day 21 Post-Wounding:** Comparing the mean of PMN inflammatory cells in both groups (Healthy and sedentary) and (diabetic and sedentary), there is a significant difference and p = 0.008 and p ++. In the exercise group, p = 0.043 and p < The control group was in the tea group and 0.002 p and * * respectively. It had a significant reduction in the control group and in the tea group with exercise, p = 0.001 and ***, indicating a decrease in meaning has been in control group and shows the effectiveness of co- infusion with tea in reducing inflammation.

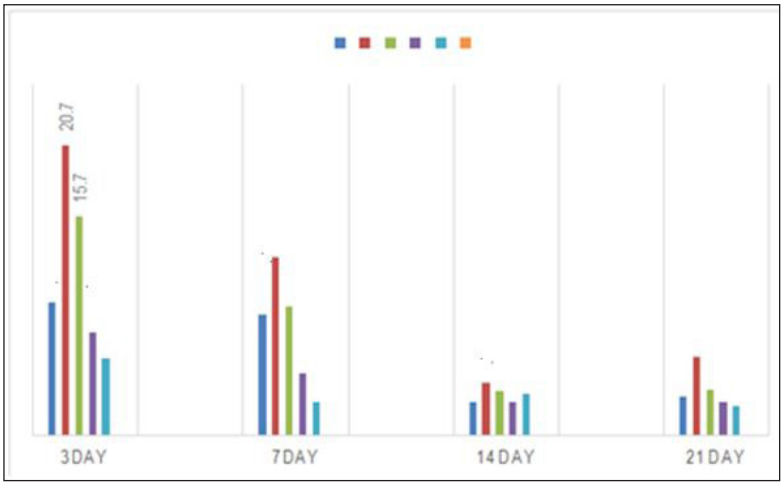


Diagram 12: Average cell (PMN) on different days post-wounding

Experience 5:

- **Day 3 Post-Wounding:** By comparing the mean number of macrophages between two groups (Healthy and sedentary) and (diabetic and sedentary), no significant difference was observed; therefore, other groups were excluded.
- **Day 7 Post-Wounding:** By comparing the mean number of macrophages between two groups (Healthy and sedentary) and (diabetic and sedentary), there is a significant difference of p = 0.023 and so the other groups are as follows: in the exercise group, p = 0.11 and ** and there was a significant increase in relation to the control group. In the teas group, p = 0.001 and p <0.001 and significant increase compared to the control group. In the tea group, P = 0.02 and p There is a meaningful relationship with the control group. This confirms that the inflammation process has been shortened in the experimental group and the cellular synthesis and restoration stages have begun earlier.
- **Day 14 Post-Wounding:** After comparing the mean number of macrophages in both groups (Healthy and sedentary) and (diabetic and sedentary), no significant difference was observed, so other groups were prevented.
- **Day 21 Post-Wounding:** By comparing the mean number of macrophages between two groups (Healthy and sedentary) and (diabetic and sedentary), there is a meaningful difference of p = 0 and +2 + respectively. Therefore, the other groups are as follows: in the exercise group, p *** and had a significant reduction in the control group. In the teas group, p = 0 and p = 0, there was a significant decrease compared to the control group. In the tea group, p = 0/0 and p * and significant reduction with the control group. This confirms that the effect of exercise and chai on wound healing has been more effective.

Average cell (macrophage) on different days post-wounding				
Test groups	**Day 3**	**Day 7**	**Day 14**	**Day 21**
Healthy + Sedentary	1.10 ± 0.73	5 ± 1.63	3.20 ± 0.78	1.90 ± 1.10
Diabetic + Sedentary	1.80 ± 1.54	2.80 ± 1.13	3.70 ± 1.05	5.61 ± 1.07
Diabetes + Exercise	1.71 ± 2.40	5.20 ± 1.68	2.50 ± 1.08	1.90 ± 1.19
Diabetes + tea	4.50 ± 1.58	5.80 ± 1.54	1.90 ± 0.73	2 ± 1.24
Diabetes + tea + Exercise	5.50± 3.50	6.90 ± 1.72	1.20 ± 0.63	0.7 ± 0.67

Table 5: Average cell (macrophage) on different dayspost-wounding

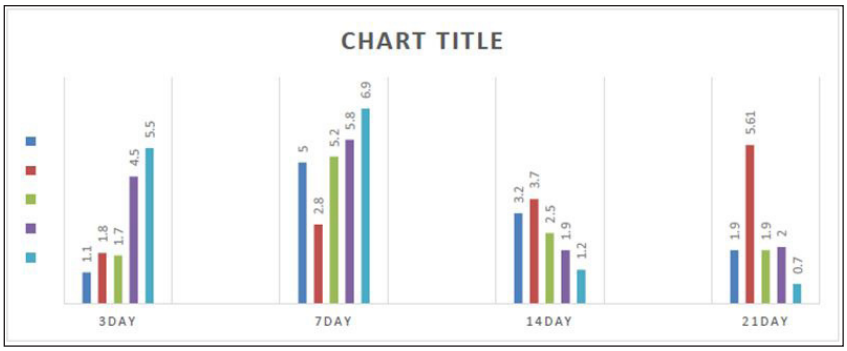


Diagram13: Average Cell (Macrophage) on Different Days Post-Wounding

Blood glucose comparison in laboratory mice: blood glucose has been measured on different days, but because there is no significant difference between healthy and non-healthy individuals, other groups can be prevented.

Weight Comparison in Laboratory Mice: There was a change in the weight of the mice, but no significant differences were found between the Healthy and the other groups and the other groups.

Discussion

Increasing oxygen supply through aerobic exercises on the treadmill examines wound healing in diabetic mice using streptozotocin. One of the most important factors in the process of wound healing is the use of medicinal herbs such as green tea extract. These medicinal herbs and also because of the presence of antioxidants, which are 100 times more effective than vitamin C and 25 times more effective than vitamin E. Today the effect of green tea extract on skin ulcers, burns, anticancer effects, rejuvenation, Alzheimer's treatment ... has been proven. There are 150 reports from in-vivo in-vitro studies on the effects of green tea on the skin. The primary focus of these studies is on chemical deterrents, chemical carcinogens or photo carcinogens in rodents [17]. Generally, glycoprotein has different biological activities, such as anti-tumor activity, anti- inflammatory, antiviral, anticoagulant, anti-aging and lowering sugar 47). The chemical structure of these molecules is green tea polyphenols, which initiates the antioxidant hypothesis [18,19]. EGCG (Epigaloccatin Galate) is the main component of polyphenolic green tea that has antioxidant, anti-tumor and anti-antigens Is mutagenic) [17]. Biological and epidemiological studies have shown in recent years that EGCG can inhibit the growth of the tumor of the lung, liver, pancreas, stomach, pancreas, skin, and prostate bladder [18]. EGCG inhibitors of chymotrypsin, a factor in tumor necrosis alpha, glucose 6- Liver phosphatase, non-acceptance of transplantation in humans and lipid peroxidase [18,20].

This change suggests that green tea has caused the inflammation of the healing process to go earlier and reach its own end and instead begin the process of reproduction. In addition, the use of green tea extract and ointment caused a significant increase in fibrosis and decrease in inflammation on the 7th day of study compared to the control group. This significant increase in the fibrosis of the treatment group, considering their role in the following, is considered to be significant, indicating the positive effect of green tea extract on the proliferation phase of the healing process of the wound:

1. Fibroblasts synthesize some of the primary extracellular matrix components of the wound bed, such as fibronectin and proteoglycans, which provide a suitable substrate for the migration and proliferation of cells [21].
2. Fibroblasts further synthesize collagen, which causes tensile strength in the wound bed [22].
3. Myofibroblasts, which are specific fibroblasts, contribute to the contraction of the wound by producing contractile force [21].

During the formation of granule tissue, fibronectin provides a suitable substrate for migratory and tubular infiltration, and also interacts with myofibroblasts, in order to effectively improve the contraction of the wound. In addition, fibronectin is considered to be the basis of fibrilligenesis (Young SF 1990). According to the above results, it has been found that the green tea extract with the healing effect of wound has been improved as of the seventh day, which also affects the reduction of surface area, increases the percentage of recovery, and reduces the time needed for complete wound healing. In other words, Inhibition of inflammation and modulation in the inflammatory stage, accelerated the wound phase. In 2004 Bayer and colleagues showed that polyphenols inhibit gamma interferon secretion and had anti-inflammatory, anti-aging and healing effects [18]. Other researchers showed that polyphenols induced differentiated and proliferated cells in epidermal keratinocytes [17]. Catechins are also a category of polyphenols that have antioxidant and anticoagulant properties and contribute to preventing bleeding and decreasing thrombosis. As of the Seventh day, the process of reproduction is considered [19,23].On the 7th day of the present study, in the treatment group, the amount of fibrous, as compared to the control group, which confirms the beginning of the regeneration phase [21]. On the other hand, the early onset of the collagen renewal phase occurred at this stage, and collagen groups with a larger diameter and transverse molecular attachments Collagen is altered [24]. Collagen fibers make the wound look similar to the original tissue before the injury, and prevent the formation of white scurvy and ugly. The research shows that green tea can reduce blood sugar, blood lipids, blood pressure, cardiovascular diseases, heart rate, and also vasodilatation [1,8]. This affects the practical capacity of fibroblasts, increases the synthesis of collagen fibers, and increases the resistance of the wound due to increased collagen content and since fibroblasts are responsible for creating collagen fibers.

Exercise also boosts vascularity and enhances oxygenation. Therefore, it can be concluded that green tea (polyphenol catechins and EGCG) causes proliferation of fibroblasts and affects the functional capacity of fibroblasts and increases the ability to synthesize collagen fibers [1,19]. A study by Madham et al. in 2007 found that catechins of polyphenol and EGCG all inhibited collagenase activity against collagen. In fact, catechin and EGCG, by binding to hydrogen, and hydrophobic interactions with collagenase, inhibit its activity and play a role in collagen stabilization [24].Young and colleagues in 2008 also investigated collagen degradation inhibition and collagenase activity through EGCG cell signaling responses, suggesting that many common and local factors are affected [25]. Many neuronal and hormonal factors, such as cellular and vascular factors, or motor and secretion activity, affect the wound area. In this regard, the effect of EGCG and the antibacterial and antiviral properties of green tea can be considered in order to accelerate healing of the wound [14,25]

In patients, wound healing is stopped at the stage of fibroplasia. In this case, although the number of fibroblasts is normal, they do not produce sufficient collagen. Vitamin C is required for OH-ion binding with proline and lysine and their hydroxylation in fibroblast cells. Without hydroxyl lysine, collagen fibers do not cross-fit. On the other hand, vitamin C is required for capillary formation, macrophage migration, and the proper functioning of neutrophils [26]. Researches have shown that green tea is a source of vitamin C and contains 18 amino acids, including lysine and propylene [17,20,25]. The deficiency of vitamin B6 (pyridoxine) damages the cross-linking of collagen in this process. The deficiency of vitamin B2 (riboflavin) causes the wound healing process to be affected [27]. On the other hand, group B vitamins are responsible for cofactor enzymatic reactions and are essential for the proper functioning of white blood cells and the formation of antibodies [26]. The results have shown that green tea and vitamin B1, B2, B620 are more effective [28-47].

References

1. Coffy RJ, Derynck JR, Wilcox JN, Bringman TS, Goustin AS, et al. (1987) Production and auto-induction of transforming growth factor in human keratinocytes. Nature 328: 817-20.

2. Olive JL, Miller GD (2001) Differential Effects of Maximal- and Moderate-intensity Run on Plasma Leptin in Healthy Trained subjects. Nutrition 17: 365-9.

3. Teixeira de Lemos, Edite, Oliveira,Jorge, Pinheiro, et al. (2012) Regular Physical Exercise asa Strategy to Improve Antioxidantand Anti- Inflammatory Status:Benefits in Type 2 Diabetes Mellitus. Oxid Med Cell Longev 2012: 741545.

4. Jeanette SJ, Alex KH, David J B (2003) Diabetes, oxidative stress and antioxidant. J Biochem Mol Toxical 17: 24- 380.

5. Atkinson MA, Maclaren NK (1994) The pathogenesis of insulin dependent diabetes. N Engl J Med 331: 1428-1436.

6. Shapiro K, Gong WC (2002) Natural products used for diabetes. J Am Pharmacol Assoc 42: 217-26.

7.Weisburger JH, Chung FL (2002) Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. Food Chem Toxicol 40: 1145-54.

8. Benelli R, Venè R, Bisacchi D, Garbisa S, Albini A (2002) Anti-invasive effects of green tea polyphenol epigallocatechin-3-gallate (EGCG), a natural inhibitor of metallo and serine proteases. Biol Chem 383: 101-5.

9. Lind L (2003) Circulating markers of inflammation and atherosclerosis. Atherosclerosis 169: 203-14.

10. Kasahara T, Kato T (2003) Nutritional biochemistry: A new redox cofactor vitamin for mammals. Nature 422: 832.

11. Duffy SJ, Vita JA (2003) Effects of phenolics on vascular endothelial function. Curr Opin Lipidol 14: 21-7.

12. Tripathi BK, Srivastava AK (2006) Diabetes mellitus: complications and therapeutics. Med Sci Monit 12: 130-47.

13. Frykberg RG, Habershaw GM, Chrzan JS. Epidemiology of the diabetic foot: ulceration s and amputation. 7: 273-90.

14. Caskey RC, Zgheib C, Morris M, Allukiahj M, Dorsett-Martin W, et al. (2014) Dysregulation of collagen production in diabetes following recurrent skin injury: Contribution to the development of chronic wound. Wound Repair Regen 22: 515-20.

15.Wu LY, Juan CC, Ho LT, Hsu YP, Hwang LS (2004) Effect of green tea supplementation on insulin sensitivity in Sprague-Dawley mice. J Agric Food Chem 52: 643-8.

16. Ryu OH, Lee J, Lee KW, Kim HY, Seo JA, et al. (2006) Effects of green tea consumption on inflammation, insulin resistance and pulse wave velocity in type 2 diabetes patients. Diabetes Res Clin Pract 71: 356-8.

17.Stephen H (2005) Green tea and the skin. J Am Acad Dermatol 52: 1049-59.

18. Bayer J, Gomer A, Demir Y, Amano H, Kish D (2004) Effect of green tea polyphenols on murine transplant- reactive. Clin Immunol 110: 100-8.

19. Salem MY, El-Azab NEE, Faruk EM (2014) Modulatory effects of green tea and aloe vera extracts on experimentally-induced lung fibrosis in mice: histological and immunohistochemical study. Journal of Histology & Histopathology 1: 6.

20. Babu PVA, EKambaram Sabitha K (2007) Green tea attenuates diabetes induced Maillard- type fluoresence and collagen cross- linking in the heart of streptozotocin diabetic mice. Pharmacol Res 55: 433-40.

21. Ferguson MWJ, Leigh IM (1998) Wound healing. In: Champion RH, Burn JL, Burns DA, Breathnach SM, eds. Rook/Wilkinson/Ebling text book of dermatology. Oxford: Blackwell Science Ltd. 337-55.

22. Clark RAF (1993) Biology of dermal wound repair. Dermatol Clin 11: 647-66.

23. Crockford GW, Hellon RF (1959) vascular responses of human skin to infrared radiation. J Physiol 4: 424-32.

24. Madha MB, Krishnamoorthy G, Raghavara J, Balachandran N (2007) Role of green tea polyphenols in the inhibition of collagenolytic activity by collagenase. Int J Biol Macromol 41: 16-22.

25.Young BJ, Suk CJ, Jung CY, Yong SS, Wook KS, et al. (2008) Epigallocatechin Gallate hampers collagen destruction and collagenase activation in ultraviolet-B-irradiated human dermal fibroblasts:Involvement of mitogen mitogenactivated protein kinase. Food Chem Tocicol 46: 1298-307.

26. Koopman CF (1995) Cutaneous wound healing: an overview. Otalaryngol Clin N Am 28: 835-45.

27. Adzick NS (1997) Wound healing. In: Sabiston DC, Lyerlu HK, eds. Textbook of surgery, The biological basis of modern surgical practice. 5th edition. Philadelphia: WB Sanders Company p.207-20.

28. Wu LY, Juan CC, Hwang LS, Hsu YP, Ho PH, et al. (2004) Green tea supplementation ameliorates insulin resistance and increases glucose transporter IV content in a fructose-fed mouse model. Eur J Nutr 43: 116-24.

29. Sugunal L, Chandrakasan G, Thomas K (1992) Influence of honey on collagen metabolism during wound healing in mice. J cline Biochem Nutr 13: 7-12.

30. Amit Soneja, Magdalena Drews, Tadeusz Malinski (2005) Role of nitric oxide, nitroxidative and oxidative stress in wound healing. Pharmacol Rep 57: 108-19

31. Doustar Y, Salehi I, Mohamadi M, Mohajeri D, Hashemi M (2007) Study of effects of treadmill exercise on diabetic nephropathy in mice. Medical Science Journal of Islamic University, Tehran medical unit under press.

32. Izadyar B. Effect of fandermol ointment on skin wound, healing in male mouse compared with normal saline, Baghyatallh University; 1374.

33. Khan N, Mukhtar H (2007) Tea polyphenols for health promotion. Life Sci 81: 519-33.

34. Király MA, Bates HE, Kaniuk NA, Yue JT, Brumell JH, et al. (2008) Swim training prevents hyperglycemia in ZDF mice :mechanisms involved in the partial maintenance of beta-cell function. Am J Physiol Endocrinol Metab 294: E271-83.

35. Kulaputana O, Macko RF, Ghiu I, Phares DA, Goldberg AP, et al. (2005) Human gender differences in fibrinolotic responses to exercise training and their determinant. Exp Physiol 90: 881-7.

36. Maria B, Witte MD, Adrian Barbul MD (2002) Role of nitric oxide in wound repair. Am J Surg 183 406-12.

37. Mayfield J (1998) Diagnosis and classification of diabetes mellitus: new criteria. Am J Family Physician 55: 1355-62.

38. Molan The antibacterial activity of honey. J Wound care 8: 415-18.

39. Nayak BS, Pinto Pereira LM (2006) Catharanthus reseus flowr extract has wound- healing activity in Sprague Dawley mice. BMC Complement Altern Med 6: 41.

40. Pickup JC, William G (1997) Epidemiology of diabetes mellitus. Textbook of diabetes. 2nd edn. UK: Blackwell , Oxford 3.1-3.28

41. Pold R, Jensen LS, Jessen N, Buhl ES, Schmitz O, et al. (2005) Long-term AICAR administration and exercise prevents diabetes in ZDF mice. Diabetes 54: 928-934.

42. Sigal RJ, Wasserman DH, Kenny GP, Castaneda-Sceppa CC (2004) Physical Activity Exercise and Type 2 Diabetes. Diabetes Care 27: 2518-35.

43. Snowling NJ, Hopkins WG (2006) Effects of Different Modes of Exercise Training on Glucose Control and Risk Factors for Complications in Type 2 Diabetic Patients. Diabetes Care 29: 2518-27.

44. Song HF, Chai JK, Lin ZH, Liu NF, Chen ML, et al. (2003) The process of wound healing in different skin tissue and its significance. Zhonghua Yi Xue-Za Zhi 83: 1070-4.

45. Warburton DE, Nicol CW, Bredin SS (2006) Health benefits of physical activity: the evidence. CMAJ 174: 801-9.

46. Wohaieb SA, Godin DV (1987) Alterations in free radical tissue defense mechanism in STZ induced diabetes in rat, effects of insulin treatment. Diabetes 36: 1014-18.

47. (2004) Wound care, Honey helps healing, say scientists. Healt &Medicin Week. Atlanta: 127928-934.