

## Green tea extracts clinical examination in humans' wounds healing process: A case study

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### Abstract

The purpose of this work was to bridge the gap between laboratory findings and practical, clinical applications of green tea extract. Green tea extract was clinically tested as a wound healing stimulator. In nine cases, a positive result was obtained during the treatment of various types of pathological wounds with the drainage of green tea extract, the introduction of a soaked ball into an open wound and its superficial application. Green tea extract was shown to be an effective remedy of various infectious, inflammatory, tropical and other after surgery complicated wounds in the process of recovery of injured tissues. Recovery processes were described in details including rate of regeneration process and symptomatic parameters.

**Keywords:** Tea; Wound; Recovery; Clinics

### 1. Introduction

Green tea (*Camellia sinensis*) has long been revered for its numerous health benefits [1], ranging from its antioxidant properties to its role in cardiovascular health [2]. Among its myriad applications, green tea extract has emerged as a potential therapeutic agent in the wound healing process [3,4]. Wound healing is a complex biological process involving hemostasis, inflammation, proliferation, and remodeling. Efficient healing is essential for restoring the integrity and function of damaged tissues. Traditional wound care approaches often involve antiseptics and antibiotics; however, the rise of antibiotic resistance and the need for more effective treatments have spurred interest in alternative remedies. Green tea extract, rich in polyphenols such as epigallocatechin-3-gallate (EGCG), has demonstrated promising anti-inflammatory, antimicrobial, and antioxidant properties in preliminary studies [5,6,7,8]. Green tea polyphenols, either in a mixture or in the form of purified catechins are able to increase cellular activities [9], including new DNA synthesis [10], in aged keratinocytes [11], or promote differentiation of exponentially growing keratinocytes located in the basal layer of epidermis. There may be two molecular mechanisms of regeneration of human wounds by green tea extract: 1) by promoting biological energy production and new DNA synthesis, both catechins and green tea extract "reenergize" the aged keratinocytes; thus, these compounds can presumably stimulate the regeneration of keratinocytes in aging skin; and 2) by induction of p57, keratin 1 and filaggrin expression, and activation of transglutaminase, EGCG also stimulated the differentiation of the keratinocytes found in the basal layer of the epidermis [12]. The combination of these two effects may help to accelerate wound healing and regeneration of new skin tissue, and subsequently prevent scar tissue formation. In addition, certain epithelial conditions may be amenable to treatment by topical applications of green tea polyphenols. Besides, due to their antimicrobial and anti-inflammatory (antioxidant) activity application of

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green tea polyphenols in treatment of various infectious wounds have been found to be very effective [13, 14]. Based on this literature information we suppose that green tea extract can be effectively used in treatment of wounds along with other traditionally used medications. Its application may stimulate a process of tissue regeneration and accordingly prevent scar formation during recovery process of wounds of various etiology. This clinical examination aims to bridge the gap between laboratory findings and practical, clinical applications. By assessing the effects of green tea extract on various stages of the wound healing process, this study explores its potential to reduce inflammation, promote cell proliferation, and enhance collagen deposition. The objective of the work was study of medicinal properties of green tea extract and its constituents – polyphenols for the purpose of treatment of various infectious, inflammatory, tropical and other after surgery complicated wounds in the process of recovery of injured tissues in clinical situation.

## 2. Materials and methods

### 2.1. Research Ethics

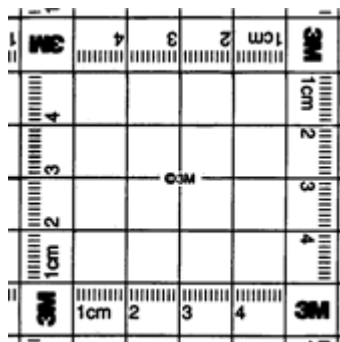
All manipulations on patients were conducted in accordance with generally accepted guidelines for use of human participants in medical experimentation, and all participants were notified about possible risks. The study was conducted in accordance with the Declaration of Helsinki 1975, (<https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/>), revised in 2013.

### 2.2. Preparation and use of green tea extract pads

0.5 to 5 g of green tea extract was dissolved in 100 to 500 ml of distilled water (we prepared 0.5% to 5% tea extract) and sterilized at 180°C for 20 minutes. Sterile dressings were impregnated with sterile green tea extract and covered the wound area as a whole and surrounding healthy tissues, if necessary, we inserted a gauze ball soaked with drainage or tea extract into the depth of the wound 3 or 5 times a day. The given concentrations of green tea extract were selected based on literature data and disease severity. It has been established that topical application of epigallocatechin gallate daily for thirty days at a concentration of 30 mg/ml was not characterized by toxicity to the skin [15].

### 2.3. Monitoring wound healing process

#### 2.3.1. Planimetric method



**Figure 1** Sterile millimetric polyethylene for measurement of wound size parameters

To determine the size, at the beginning of the treatment, we spread a sterile millimeter cellophane on the pathological open, non-healing wound (Figure 1). We drew the outline of the wound on it with ink, counting the square millimeters inside the outline, delimiting the area of the wound. To measure the depth of the wound, we inserted a sterile centimeter metal groove in the center of the wound [16].

During the regeneration period, we measured the wound parameters at 5-10-day intervals.

The relative speed of regeneration of the wound area was calculated according to formula:

$$V_{\text{rel}} = 100(S_i - S_j)/S_j N$$

Here  $S_i$  and  $S_j$  are the wound area on the  $i$ -th and  $j$ -th days, respectively.  $N = i - j$

$V$  relative was expressed as % per day.

The absolute rate of wound healing is  $V_{abs}$ . It was calculated as the change in wound area relative to the number of days in which this change occurred. Accordingly, it was expressed as  $\text{cm}^2/\text{day}$ .

The wound volume relative to its area gives us the growth rate of granulation tissue in the direction normal to the wound surface:

$$V_g = (V_i - V_j) / S_i N$$

$V_g$  is the granulation rate expressed in  $\text{cm}/\text{day}$ .

$V_i$  and  $V_j$  are wound volumes on day  $i$  and day  $j$ , respectively, expressed in  $\text{cm}^3$ . In order to calculate the volume of the wound, the shape of the wound was approximated to some geometrical figure, such as: cone, cylinder, hemisphere or sphere, and the volume was approximately calculated by the appropriate formula.

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### 3. Results and Discussion

#### 3.1. Case I: Complicated wound after ankle surgery.

A 56-year-old female patient had growths on the meta dorsal bones of the ankle after the operation, with necrosis of the edges of the wound, and a purulent wound of  $9 \times 4$  cm size was formed on the medial surface of the ankle. There was intense discharge. Against the background of antibacterial drugs, local treatment was performed, 3% hydrogen peroxide, leucine ointment, and dioxidine solution were used in a mixture. The inflammatory process decreased, as for regeneration, it was inhibited, which was manifested by the formation of weak granulation tissue, which did not heal. Despite the prescribed stimulating therapeutic drugs, the patient's treatment continued for 23 days without results. In agreement with the patient, we started treatment with 1% extract of green tea.

At the beginning of the treatment, we took the dimensions of the wound: the depth in the center of the wound was 4 cm, the area -  $49.5 \text{ cm}^2$ , and the volume -  $198.0 \text{ cm}^3$ .

Within 4 days after the start of treatment, a pink serous exudate was released from the wound, which indicates increased blood flow. On the seventh and eighth day, the healing of the granulation tissue was observed, which was manifested in its active growth. The depth in the center of the wound was 2 cm, the area was  $21.7 \text{ cm}^2$ , and the volume was  $43.4 \text{ cm}^3$ . On the 16th day, the depth in the center of the wound was 1.2 cm, the area was  $6.4 \text{ cm}^2$ , and the volume was  $7.68 \text{ cm}^3$ .

On the 30th day, overgrowth of tissue was noted locally in various places of the wound, which was inhibited by lapis pencil. The wound healed without a scar.

#### 3.2. Case II: Traumatic wound in the posterior medial part of the femur on the surface.

A 37-year-old male patient developed a laceration on the posterior medial surface of the thigh due to trauma. In the depth of the wound, bruised-crushed fatty tissue and venous bleeding were observed. The wound was processed surgically, stitches were applied, an operation was performed. After the operation, the situation became complicated. The patient had a metabolic disorder, anemia, a sharp decrease in albumin and nitrogenous substances. Therefore, tissue regeneration in the wound was inhibited, which was manifested in the spontaneous opening of the wound edge after removing the sutures (Figure 2).



**Figure 2** Tissue regeneration was inhibited due to the lack of nitrogenous substances in the body. The wound did not heal.

No pathological microbe was found by microbiological analysis. Along with the complex treatment, the patient was prescribed local medicines for the wound, which contribute to the recovery and regeneration of cells and tissues: Solcoseryl jelly 3 times a day and 10% methyluracil ointment.

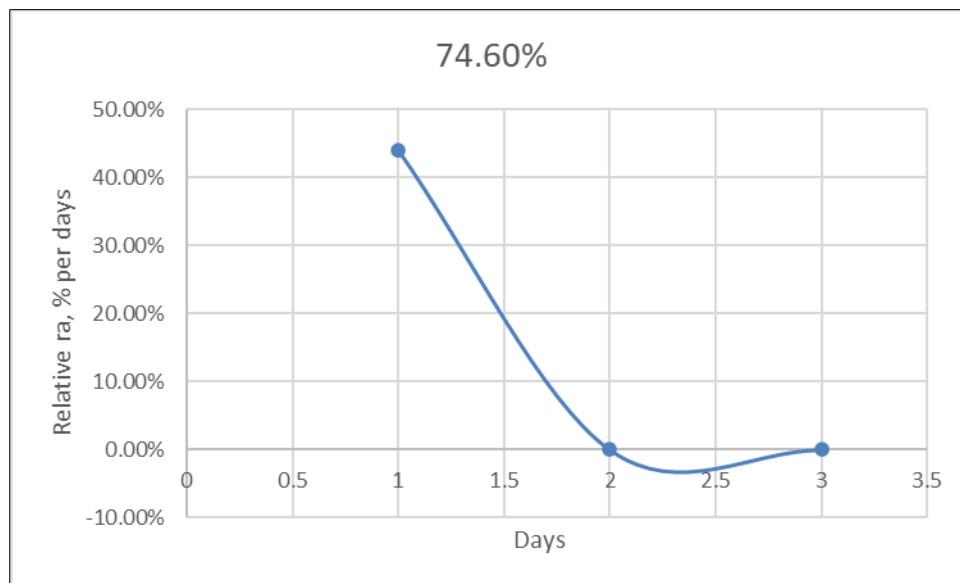
A positive result was not obtained within twenty-nine days of the treatment.

In agreement with the patient, green tea extract was included in the healing process. Before starting the experiment, we measured the dimensions of the wound. The depth of the wound in the center was 5 cm. area - 33.6 cm<sup>2</sup>. volume - 168.0 cm<sup>3</sup>. We inserted a ball soaked in 4% tea extract into the wound, and covered the wound area as a whole and the surrounding healthy tissues with a pad soaked in tea solution 5 times a day. On the second and third day after the application of the tea extract, a pink serous exudate was observed from the wound, which indicated increased blood flow. On the fifth day after the start of the experiment, the discharge decreased, on the sixth day it stopped. On the ninth day, a pale granulation tissue appeared in the corners of the wound. On the 16th day, the amount of granulation tissues increased intensively (Figure 3).

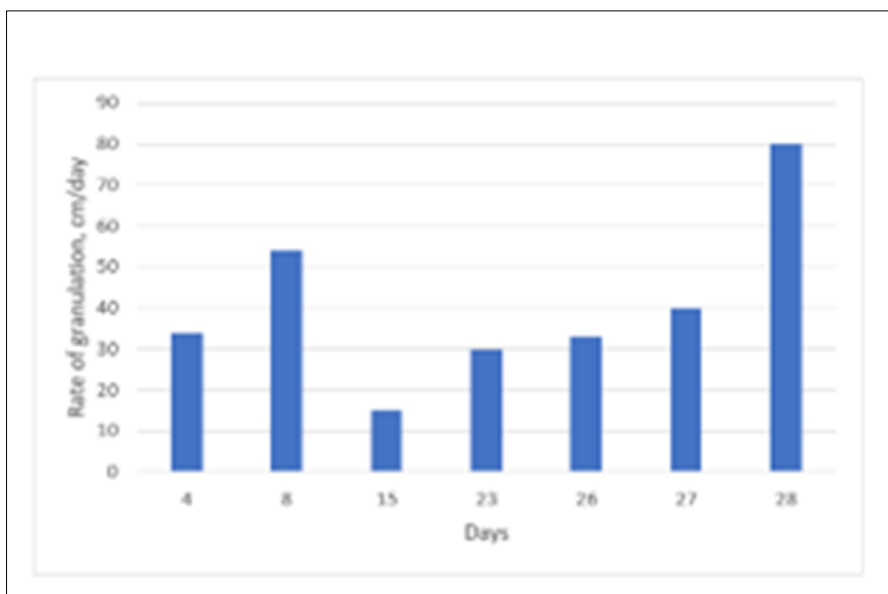


**Figure 3** On the 16th day in the background of tea extract treatment. The depth of the wound was drastically reduced.

On the background of treatment, the size of the wound decreased. On the 16th day, the depth of the wound in the center was 2.5 cm, the area was 20.8 cm<sup>2</sup>, and the volume was 52.0 cm<sup>3</sup>. On the 24th day, the depth of the wound in the center became 0.5 cm, the area - 0.78 cm<sup>2</sup>, and the volume - 0.39 cm<sup>3</sup>. Relative rate changes are shown in Figure 4. On the 30th day, the wound depth was 0.2 cm. Changes in granulation rate is presented in Figure 5. The treatment lasted 30 days.



**Figure 4** Changes in the relative rate of wound healing according to days.



**Figure 5** Changes in rate of granulation, case II

### 3.3. Case III: foreign body injury Infected wound on lower leg

A 70-year-old female patient received an injury in the lower part of the tibia - a foreign body puncture wound. The wound became infected. At the beginning of the treatment, the wound was processed surgically, stitches were placed, complex treatment was prescribed. The situation became complicated on the 5th day. The wound swelled, necrotic tissue appeared around it, suppurated, the stitches opened. The wound was treated daily with 3% hydrogen peroxide and antiseptics.

The wound was drained. Treatment for eleven days was unsuccessful (Figure 6).



**Figure 6** An infected wound in the lower lag did not heat after long-term treatment

Along with the complex treatment, the patient was prescribed a 1% extract of green tea. From the swab taken from the wound, the bacteria of *Staphylococcus aureus* were isolated. We injected the tea extract into the wound with drainage, and at the same time we covered the entire wound area and the surrounding healthy tissues with a tea extract-soaked pad. On the fourth day after the start of the experiment, the swelling decreased sharply. Tea extract induced spontaneous removal of dead necrotic tissues. On the 9th day, the wound was cleaned. On the 13th day after treatment, a pale granulation tissue appeared in the corners of the wound. At the beginning of the treatment, the depth in the center of the wound was 2 cm, the area was 23.4 cm<sup>2</sup>, and the volume was 46.2 cm<sup>3</sup>. On the 15th day, the size of the wound decreased: the depth became 0.50 cm, the area 2.4 cm<sup>2</sup>, and the volume 1.2 cm<sup>3</sup>. On the 25th day, the wound was almost closed.

### 3.4. Case IV: Osteotomy of the tibia.

A 55-year-old male patient developed an obliterating endarteritis with angular curvature of the right tibial false joint after some time due to trauma. An operation was performed - osteotomy of the tibial bone, at the level of the false joint of the diaphysis of the small tibial bone. After the operation, the condition became complicated: a subacute ongoing osteomyelitis of the tibia developed, which took on a chronic character despite antibacterial anti-inflammatory therapeutic treatment. An osteomyelitis ulcer gradually formed on the medial side of the tibia in the area of the operation, the bottom of which was formed by the necrotic ends of the same bone fragments. Complex treatment was used along with wound necrotomy and surgical treatment. The wound area was treated with antiseptics: 96% alcohol, iodine, 3% hydrogen peroxide, a tampon soaked in a mixture of 1% dioxidine and Leosons' ointment was inserted into the wound 3 times a day. Clinical blood analysis showed leukocytosis, low hemoglobin. Despite the long complex treatment, they did not get a positive result. In agreement with the patient. We included 5% green tea extract in the treatment process. We spread a wet pad over the entire wound area and surrounding healthy tissues.

At the beginning of the experiment, we took measurements of the wound. The depth in the center of the wound was 4.2 cm, the area was 4.6 cm<sup>2</sup>, and the volume was 19.4 cm<sup>3</sup>. Staphylococcus aureus bacterium was isolated from the wound. Pink serous exudate was observed within 4 days after the start of treatment. The ulcer in the wound area completely disappeared on the 6th day. On the 7th day, the depth in the center of the wound decreased to 3.5 cm, the area - to 1.8 cm<sup>2</sup>, and the volume - to 6.4 cm<sup>3</sup>. On the 10th day, the depth in the center of the wound was 2.3 cm, the area was 0.75 cm<sup>2</sup>, and the volume was 1.7 cm<sup>3</sup>.

The tea treatment was stopped because the tissue growth was going on intensively. The patient was discharged home in a few days.

The situation was complicated because he used a home-made ointment for treatment. The wound became infected, swollen. A hole with a diameter of 5 mm appeared on the tibia. We used 5% tea extract again.

At the beginning of the treatment, the depth of the wound in the center was 3.8 cm, the area was 7.2 cm<sup>2</sup>, and the volume was 27.4 cm<sup>3</sup>. Pinkish exudate increased from the wound. The swelling decreased, but within 20 days we did not get a positive result, no regenerative tissue was formed in the wound. After that, we put 1% extract of catechins from green tea into the wound. We applied the extract in the wound with a wet ball and, also, applied a wet pad on top of the 1 cm<sup>2</sup> area 6 times a day. Within 3 days after the release of pink serous exudate increased, which indicated the restoration of blood circulation. On the 5th day, a visually visible filamentous fibrinolytic formation, approximately 7 mm long, branched at the ends, developed at the corner of the wound. On the eighth day, the first light-colored granulation tissue 8 mm appeared behind the fibrin thread. On the 12th day, the depth of the wound became 2.7 cm, the area 4.56 cm<sup>2</sup>, and the volume 12.3 cm<sup>3</sup>. On the 14th day, the length of the granulation tissue increased to 8-10 mm. On the 17th day, the emerging tissue reached the dimensions of 1.8X1.3 cm. Tissue growth was intensive, but bone tissue growth did not occur due to the background of chronic osteomyelitis.

### 3.5. Case V: Anterior abdominal wall abscess.

A 59-year-old female patient was dissected under anesthesia, an abscess of the anterior abdominal wall was opened, according to X-ray examination, it was about 7 cm, and 0.9 milligrams of dirty yellow pus with a strong sweet smell was released. Abscess pockets were opened by revision of the finger - pyogenic capsule, roughened, thickened. The abscess cavity was washed with 3% hydrogen peroxide. By microbiological analysis, sticks of blue-green suppuration - Pseudomonas aeruginosa - were isolated. The cavity was drained. There was an excess of leukocytes in the blood, the temperature was 39.5 °C. The treatment was complex. The wound was washed with antiseptic substances with drainage means. Eleven days after the start of the treatment, no positive results were obtained. The patient had a high temperature, 39 °C.

In agreement with the patient, we introduced 40 grams of 3% green tea extract into the wound through drainage, 3 times a day. For four days after the start of treatment, a large amount of fibrous-purulent discharge was released from the wound through drainage. During administration of the tea extract, the patient had a gnawing pain in the target point in the abdomen for 10-15 minutes. On the ninth day, the discharge from the wound decreased, the temperature dropped to 36.8 °C, the number of leukocytes in the blood decreased to the normal range. The depth of the wound increased, which was caused by the purulent mass being pushed out and the total disintegration of the pyogenic capsule. On the 15th day, there was practically no discharge from the wound, on the 18th day we removed the drainage. The wound was closed five days after the drain was removed. On the 23rd day, an X-ray examination was performed - a small cavity was noted, clinical and biochemical data were within the norm.

### 3.6. Case VI: Complicated in the postoperative period infected wound.

A 44-year-old male patient underwent an acute appendectomy. The patient's condition was complicated by peritonitis in the postoperative period. After a long treatment, he was discharged with an open wound. The patient was treated with curiosin solution on the open wound for twenty-five days, but he did not get a positive result. Tissue regeneration was inhibited. In agreement with the patient, we started the treatment with a 4% extract of green tea. We inserted a ball soaked in tea extract into the wound and applied a wet pad to the wound area as a whole, including the healthy tissues surrounding it, 3 times a day. At the beginning of the experiment the depth in the center of the wound was 3 cm, the area was 7.98 cm<sup>2</sup>, and the volume was 23.94 cm<sup>3</sup>. Within three days of starting treatment, a serious pink exudate was observed in the wound. On the fifth day, the discharge decreased. On the 7th day, faint granulation tissues developed at the edges (corner) and depth of the wound. On the 9th day, the granulation tissue grew intensively. On the 12th day, the depth of the wound in the center was 1.1 cm; the area was 1.2 cm<sup>2</sup>, and the volume was 1.32 cm<sup>3</sup>. On the 15th day, the depth of the wound in the center became 0.50 cm. The area was 0.7 cm<sup>2</sup>, and the volume was 0.35 cm<sup>3</sup>. On the 20th day, the wound was closed without a scar.

### 3.7. Case VII: Adenectomy in the postoperative period, complicated wound.

A 75-year-old male patient underwent a one-time adenectomy leaving an epicystic drainage. The episiotomy wound became complicated, opened, and formed a cavity. Along with the complex treatment, surgical treatment of the wound with antiseptic agents was carried out. No positive results were obtained within twenty-eight days. Wound healing did not occur because tissue regeneration was inhibited. The patient had a skin disease, which made it difficult for new tissue to form and grow. We started treatment with a 4% extract of green tea. Microbiological analysis did not show any pathogenic microbe. We applied tea extract to the wound with a ball soaked in tea extract and applied a wet pad to the entire wound area and the surrounding healthy tissues 4 times a day.

Before starting the experiment, we took the dimensions of the wound: the depth in the center of the wound was 3.4 cm, the area was 2.04 cm<sup>2</sup>, and the volume was 6.93 cm<sup>3</sup>.

A pink exudate was observed in the wound for three days after the start of treatment. On the fifth day, discharge stopped. On the twelfth day, the depth of the wound in the center decreased to 0.3 cm, the area was unchanged, and the volume was 0,63 cm<sup>3</sup>. No granulation tissue was seen superficially.

Growth process, the granulation of new tissue, took place from the depth of the wound, as evidenced by a reduction in the size of the depth of the wound. On the twenty-second day, the wound healed without a scar.

### 3.8. Case VIII: Infected ankle wound.



**Figure 7** An abscess of foreign etiology on the ankle

A 57-year-old female patient had an abscess of foreign etiology on her ankle. The bacteria of *Staphylococcus aureus* were isolated by microbiological analysis. In agreement with the patient, the treatment consisted of green tea with 0.5% extract. We covered the whole area of the wound and the surrounding healthy tissues with a pad soaked in tea extract

4 times a day. From the beginning of the treatment, a serous pink discharge was observed in the wound for 4 days (Figure 7).

On the 8th day, the damaged tissues begin to recover. The pus disappeared. Tissue regeneration was going on intensively. When the new tissue was attached to the epidermis, we inhibited it with a lapis pencil. On the 15th day, the wound was closed.

### **3.9. Case IX: A 47-year-old male patient was operated on - resection of the small intestine, suturing of the damaged segment.**

The operation was complicated: suppuration of the wound; diastasis (wide opening of the wound), small fistula. The patient received corticosteroids for 18 years due to immunodepression, the repair was prolonged due to sluggish wound regeneration and weak granulation. There was an infection of the wound, with a strong odor. *Staphylococcus aureus* was isolated during microbiological inoculation of the smear. The patient was hospitalized for 46 days. We treated the wound with antiseptics 2 times a day, and administered antibiotics. Due to the complication of the condition, we included 5% green tea extract in the treatment in agreement with the patient. Drainage of gauze soaked in the extract was inserted into the wound for 30-50 cm in different directions, in the area of the epigastrium, three times a day.

Result: when the green tea extract was applied to the wound, the patient had a mild dull pain for an hour. On the second day after the start of the treatment, the deodorizing action of the solution was clearly manifested. On the fourth day, the necrotic tissue in the wound began to slough, the color was yellowish-green. On the eighth day, the wound was cleaned, an excess of granulation tissue was observed. which ultimately significantly accelerated wound recovery and epithelization. He was discharged on the fourteenth day.

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## **4. Conclusion**

Green tea extract is an effective remedy of various infectious, inflammatory, tropical and other after surgery complicated wounds in the process of recovery of injured tissues. Green tea extract is much favorable treatment agent of wounds in comparison with such traditional medications as *Soution*, *Curiosin*, 10% *Ungenum Methyluracil*, *Ungenum Solcoceril*, *Ungenum Leosin*, *Ungenum Iruxsol*.

The results of this investigation could significantly impact clinical practices by introducing an effective, natural adjunct to existing wound care protocols. Additionally, understanding the bioactive components of green tea and their specific roles in tissue repair can pave the way for new therapeutic strategies in regenerative medicine.

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## **Compliance with ethical standards**

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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