

## Original Research Article

### Effect of Turmeric Extract with Zinc Oxide Nanoparticles Application on Burn Wound

#### ABSTRACT

An experiment was conducted at the Department of Physiology and Pharmacology, Hajee Mohammad Danesh Science and Technology University, Dinajpur, Bangladesh to see the clinical effectiveness of turmeric extract with **zinc oxide (ZnO)** nanoparticles to hot iron burn wound in rabbit model. Data were collected on the healing rate, healing time and **WBC** count. Sixteen male New Zealand White rabbits were divided into four groups where group  $T_0$  served as the non-treated,  $T_1$  as burn healing using turmeric extract,  $T_2$  burn heals with turmeric extract and ZnO nanoparticles; and  $T_3$  burn heals with Bactrocin®. The results showed that the  $T_2$  treatment had the best ( $93\pm0.707\%$ ),  $T_3$  better ( $88.5\pm1.04\%$ ),  $T_1$  good ( $86.5\pm1.55\%$ ) performance and while the  $T_0$  ( $67.5\pm0.86\%$ ) gave the worst performance. The  $T_3$  ( $26.5\pm0.60$ days) and  $T_2$  treatments had the greatest results ( $24.5\pm0.6455$  days) and required the fewest days of healing compared to  $T_0$  which takes maximum days ( $35.5\pm0.64$ ). The study revealed that the WBC count was maximum in non-treated group (at 0, 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> week which is ( $5600\pm31.06$ ,  $9000\pm36.47$ ,  $8000\pm38.41$ ,  $7500\pm36.11$  and  $6000\pm43.11$  cell/ul respectively). The  $T_2$  treatments showed lower WBC count during the entire studied period (0, 1<sup>st</sup> and 4<sup>th</sup> days) and  $T_3$  at (3<sup>rd</sup> week and 4<sup>th</sup> week). Overall, the results of the study showed that use turmeric extract and ZnO nanoparticles led to faster burn wound healing with a shorter time required, proving that treating burn wounds in rabbits without the use of commercial drug is both feasible and recommended for practice.

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**Keywords:** Turmeric, ZnO nanoparticles, Commercial drug, Wound, Rabbit

#### 1. INTRODUCTION

Any anatomical or physiological disruption in skin structure that results in skin cell destruction is referred to as a wound [1]. As a result, wound healing is an intricate and multifaceted process that starts as soon as skin is lost and involves the reaction and interaction of cells and mediators to restore natural skin capacity. Three overlapping and ongoing stages of wound healing include remodeling, inflammation, and proliferation [2]. In the first stage of homeostasis,

vascular constriction and clot formation brought on by fibrin and platelets stop bleeding right away after damage [3, 4].

Burn injuries cause maternal and infant mortality and morbidity. Factors affect this morbidity and mortality, including the depth and size of the burn [5]. Due to the role of flame fires and attempted suicides, practical activities such as education to decrease this awful event and its physical and emotional complications from responsible governors still seem mandatory. Due to pollution and infections at the wound site, the main worry nowadays is the delayed and poor healing of burn injuries throughout the world [6]. Over the years, a variety of medicinal herbs have also been utilized for the care and healing of wounds [7].

Turmeric (*Curcuma longa*) is a member of the ginger family (*Zingiberaceae*). It has been used since antiquity as a dye and condiment. Turmeric, sometimes called Indian saffron or the golden spice, is a tall plant that grows in Asia and Central America. In Asian countries, it has been consumed daily for centuries and no toxicity has been reported [8]. The bright yellow color of it is derived primarily from the fat-soluble, polyphenolic pigments known as curcuminoids. Curcumin (diferuloylmethane), the principal curcuminoid found in *C. longa*, is generally considered as its most active constituent. Other curcuminoids found in turmeric include bisdemethoxycurcumin and demethoxycurcumin [9]. Curcumin is the active ingredient in turmeric, and it has powerful biological properties. Turmeric has also been reported to exhibit properties like an antiseptic, cure for skin diseases, wound healing, respiratory distress, cure for poisoning, eliminate waste products from the body, and remedy for treatment of sprains and swellings caused by injury [10]. Several biological activities of curcumin have been identified, including anti-inflammatory, anticarcinogenic, anti-infectious, antioxidant, anti-apoptotic, and wound healing activities [11]. To enhance its bioavailability, curcumin has been incorporated into different formulations using hydrogel, nanoparticles, micelles, hyaluronic/oleic acid-loaded and glucosylation of the hydrophobic molecule in pre-clinical studies. It has shown potential as a wound healing agent. Turmeric has been getting attention recently because of its antioxidant abilities. The antioxidant effect of turmeric appears to be so powerful that it may protect the liver from being damaged by toxins.

Scientists are interested in a range of biomedical applications since nanotechnology is a fast expanding and complex study field [12]. The fields of industry, health, food, biomedicine, and cosmetics are only a few of the areas of life where nanoparticles have been introduced. The standard definition of a nanoparticle or ultrafine particle is a material particle with a diameter of

one to one hundred nanometers (nm). It can also refer to fibers and tubes that are smaller than 100 nm in only two directions, or bigger particles up to 500 nm in size. Nanoparticles are being used in a variety of areas of life, including the biomedical, cosmetics, food, and industrial sectors. The most intriguing inorganic metal oxides are ZnO-NPs because they are easy to prepare, affordable to produce, and clean [13].

Numerous studies have been done to show how well zinc works to heal wounds. It has been demonstrated that preparations containing zinc accelerate the healing of wounds and reduce bacterial infection at the tissue site. Additionally, they helped the wound's granulation tissue to develop [14]. ZnO is an inorganic substance that demonstrates exceptional qualities such as semiconductor, broad radiation absorption, piezoelectric, pyroelectric, and high catalytic activity. Scientists' interest in a range of biomedical applications has been spurred by the rapidly expanding and demanding field of nanotechnology [15]. Recently developed antimicrobial nanoparticles have proven to be quite helpful, especially for wound healing [16]. It has lessened acute toxicity in addition to overcoming bacterial resistance. It has also decreased the price of treatment when compared to conventional antibiotics [16]. [17] found that nanoparticles have longer-lasting therapeutic benefits than conventional antibiotics because they persist in the bloodstream for longer periods of time [17]. Hardly any research has been conducted to determine the effectiveness of the turmeric with zinc nanoparticles in rabbit. In light of the above-mentioned qualities, therapeutic applications of turmeric extract, and ZnO nanoparticles, the following experiment was conducted on rabbits to know the clinical efficacy of turmeric with ZnO nanoparticles on burn the wounds healing activity based on healing rate, healing time and WBC count.

## 2. MATERIALS AND METHODS

### 2.1 Experimental period and location

The experiment was carried out in the animal research laboratory of the department of Physiology and Pharmacology, HSTU, Dinajpur, between June 5 and July 17, 2022.

### 2.2 Collection of rabbit

At Rangpur, 16 male New Zealand White rabbits were collected when they were around 2.5 months old.

### 2.3 Experimental treatments

Sixteen male rabbits of near about 2.5 months were chosen and divided into four groups i.e. T<sub>0</sub>= non-treated group, T<sub>1</sub>= Hot iron burned and treated with turmeric extract, T<sub>2</sub>= Hot iron burned

**Comment [Ma2]:** What is the temperature of hot iron burned?

**Comment [Ma3]:** Add information on the turmeric extract. Is it in liquid or powder form? where did the author get the turmeric extract? The information should be written in the materials section.

and treated with turmeric extract and ZnO-NPs and T<sub>3</sub>= Hot iron burned and treated with commercial drug (Bactrocin®)

**Comment [Ma4]:** Add information on the ZnO-NPs. The nanoparticle size, where did the author get the ZnO-NPs? The information should be written in the materials section.

#### 2.4 Collection and preparation of extract

The HSTU campus is where the turmeric was collected. The sample preparation was followed by [18].

**Comment [Ma5]:** Add information on the Bactrocin. Where did the author get the Bactrocin? The information should be written in the materials section.

#### 2.5 Combined used of turmeric extract and ZnO-NPs

The gel was made by combining 4g turmeric and 1g ZnO. Then, this mixture was utilized in the hot iron burn wound positions twice daily [19].

**Comment [Ma6]:** Explain in detail the step mixing process.

#### 2.6 Data Collection

##### 2.6.1 Recording of wound healing time

Any formation of the scare was also noted carefully as the sign of healing at the time interval of 7 days for each treatment group.

**Comment [Ma7]:** Show the image evidence on the formation of scare. Is there any tool to identify and measure the scare?

##### 2.6.2 Determination of healing rate

Every treatment group's recovery rate was assessed after a 7-day break. It was computed by dividing the time needed to completely close the wound by the largest average wound margin distance from the wound center. The following formula was used to determine the healing rate at weekly intervals:

$$\text{Wound Closure (\%)} = \frac{[(\text{Area of the wound on day 0} - \text{area of the wound on indicated day}) / \text{Area of the wound on day 0}] * 100}{[20]}$$

##### 2.6.3 Determination of healing time

From the day the wound was first created until the research's end day count, the rabbit's recovery time was determined. The recovery time was calculated for each treatment group on a weekly basis. [Room temperature & condition?](#)

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##### 2.6.4 Determination of WBC enumeration

WBC count were carried out by Automated Mindray BC-10 Haematology Analyzer and done manually at Green diagnostic center, Dinajpur. The WBC was count for each treatment group every week.

#### 2.7 Statistical analysis

Microsoft Excel and SPSS version 22 were used to calculate the findings of several biochemical parameters. Analysis of variance was used to identify variations between group means that were statistically significant (ANOVA).

### 3. RESULTS AND DISCUSSION

### 3.1 Wound Healing Rate (%)

The healing rate of the burn-injured rabbits was shown in Table 1 to have steadily increased from the first to the fourth week of the study period and to have significantly varied between the experimental treatments ( $P < 0.01$ ). The  $T_2$  treatment group (turmeric extract with ZnO nanoparticles) showed the highest healing rate ( $93 \pm 0.707$ ), followed by the  $T_3$  treatment group ( $88.5 \pm 1.04$ ), the  $T_1$  treatment group ( $86.5 \pm 1.55$ ), and the  $T_0$  treatment group ( $67.5 \pm 0.86$ ). Among the investigated therapies, the  $T_2$  (turmeric extract with ZnO nanoparticle) treated group displayed the best results in terms of healing rate over the course of the entire study (1<sup>st</sup> week to 4<sup>th</sup> week). Previous investigations have shown that the well-known antibacterial compound ZnO is effective at very low bacterial concentrations. The biosynthesized ZnO from turmeric plant extract has also been shown to have antibacterial properties due to its tiny size, which offers a high surface area and increases interaction between the NPs and the bacterial cells. This is in line with [21], which showed that the biosynthesis was effective against a variety of bacteria and fungi, including *Staphylococcus aureus*, *Serratia marcescens*, *Proteus mirabilis*, and *Citrobacter freundii*. These improved healing rates compared to other treatments.

**Comment [Ma8]:** Any bacterial concentration analysis for this work?

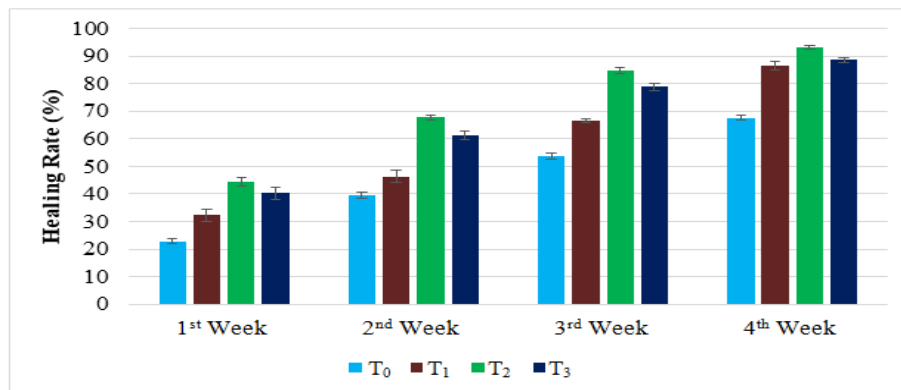
**Comment [Ma9]:** Term "tiny" is not suitable. May change to nanosize

**Table 1: Effects of turmeric extract, turmeric extract with ZnO nanoparticles and Bactrocin® on hot iron burn wound healing rate (%) of rabbit weekly**

Treatment	1 <sup>st</sup> Week	2 <sup>nd</sup> Week	3 <sup>rd</sup> Week	4 <sup>th</sup> Week
$T_0$	$22.75 \pm 0.94^a$	$39.5 \pm 1.04^a$	$53.75 \pm 1.25^a$	$67.5 \pm 0.86^a$
$T_1$	$32.25 \pm 2.28^b$	$46.25 \pm 2.17^b$	$66.5 \pm 0.64^b$	$86.5 \pm 1.55^b$
$T_2$	$44.25 \pm 1.49^c$	$67.75 \pm 0.94^d$	$84.75 \pm 1.25^d$	$93 \pm 0.707^c$
$T_3$	$40.25 \pm 2.32^c$	$61.25 \pm 1.49^c$	$78.75 \pm 1.18^c$	$88.5 \pm 1.04^b$
P-Value	0.000***	0.000***	0.000***	0.000***

\*\*\* Significant at 1% level, Mean for wound recover size with different superscript within the rows were significantly different at  $p < 0.01$ .

Here,  $T_0$ = Control/non-treated group,  $T_1$ = Hot iron burned and treated with turmeric extract,  $T_2$ = Hot iron burned and treated with turmeric extract and ZnO-NPs,  $T_3$ = Hot iron burned and treated with Bactrocin®



**Figure 1:** Effects of turmeric extract, turmeric extract with ZnO-NPs and Bactrocin® on hot iron burn wound healing rate (%) of rabbit

Comment [Ma10]: Please explain and state "Figure 1" in the main text

Here, T<sub>0</sub>= Control/non-treated group, T<sub>1</sub>= Hot iron burned and treated with turmeric extract, T<sub>2</sub>= Hot iron burned and treated with turmeric extract and ZnO-NPs, T<sub>3</sub>= Hot iron burned and treated with Bactrocin®

### 3.2 Healing Time

Table 2 showed the healing time requirements (days) of the different treatments during the study period. The result of the study showed significant variation among the experimental treatments ( $P < 0.01$ ). The T<sub>3</sub> (commercial medicine Bactrocin) treatment ( $26.5 \pm 0.60^a$ ) and T<sub>2</sub> (Turmeric extract) treatments had the best results ( $24.5 \pm 0.6455^a$ ) and required the fewest days of healing compared to other treatments for the rabbit's artificially hot iron burned wound. The T<sub>0</sub> (control) treatments takes maximum days ( $35.5 \pm 0.64^c$ ) than other treatments to heal the artificial burn wound of rabbit. On the other hand, the control group takes the maximum days to settle the artificial burn wound of the rabbits. The glycolysis process, which includes converting carbohydrates into energy, is one potential method of interaction between Zn<sup>±</sup> ions and plant phytochemicals. These interactions result in the fastest and highest healing of the rabbit's burn wound[22]. The mechanism of action of turmeric extract in wounds is by inhibiting the enzymes cyclooxygenase (COX-2) and lipooxygenase (LOX), which play a role in the inflammatory process, accelerating tissue re-epithelialization, cell proliferation, and collagen synthesis. It improves the healing process rapidly.

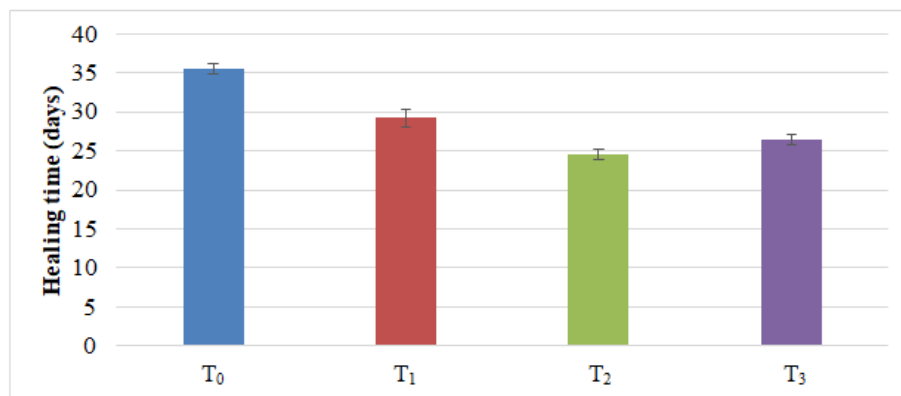
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**Table 2: Effects of turmeric extract, turmeric extract with ZnO nanoparticles and Bactrocin® on hot iron burn wound healing time of rabbit at 4<sup>th</sup> week**

Treatment	Healing Time (Days)
T <sub>0</sub>	35.5±0.64 <sup>c</sup>
T <sub>1</sub>	29.25±1.10 <sup>ab</sup>
T <sub>2</sub>	24.5±0.6455 <sup>a</sup>
T <sub>3</sub>	26.5±0.60 <sup>a</sup>
P-Value	0.000***

\*\*\* Significant at 1% level, Mean for wound recover size with different superscript within the rows were significantly different at p<0.01.

Here, T<sub>0</sub>= Control/non-treated group, T<sub>1</sub>= Hot iron burned and treated with turmeric extract, T<sub>2</sub>= Hot iron burned and treated with turmeric extract and ZnO-NPs, T<sub>3</sub>= Hot iron burned and treated with Bactrocin®



**Figure 2: Effects of turmeric extract, turmeric extract with ZnO nanoparticles and Bactrocin® on hot iron burn wound healing time of rabbit at 4<sup>th</sup> week**

Comment [Ma11]: Please explain and state "Figure 2" in the main text

Here, T<sub>0</sub>= Control/non-treated group, T<sub>1</sub>= Hot iron burned and treated with turmeric extract, T<sub>2</sub>= Hot iron burned and treated with turmeric extract and ZnO-NPs, T<sub>3</sub>= Hot iron burned and treated with Bactrocin®

### 3.3 WBC count

The WBC Count cells/ul of the various researched treatments, which is considerably influenced by the various experimented groups, is shown in Table 3 (P<0.01). The WBC count (cells/ul) was significantly higher in the control group (P<0.01), followed by T<sub>1</sub> (single Turmeric extract) treatment. The present study revealed that the WBC count was greatly increased in non-treated treated group (at 0, 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> week) which is (5600±31.06<sup>d</sup>, 9000±36.47<sup>d</sup>, 8000±38.41<sup>c</sup>, 7500±36.11<sup>d</sup> and 6000±43.11<sup>d</sup> respectively). The T<sub>2</sub> treatments showed lower WBC count during the entire studied period (0, 7 and 28 days) and T<sub>3</sub> at (3<sup>rd</sup> week and 4<sup>th</sup>

week).Administration of curcumin resulted in decreases in the size of the burn wounds and a reduction in inflammation [23]. Turmeric also provides antioxidant effects by restoring an imbalance between the production of ROS (free radicals) and antioxidant activity. In the proliferative phase, curcumin can produce collagen synthesis of fibroblast migration, vascular density, and epithelialization([add reference to support this statement](#)).

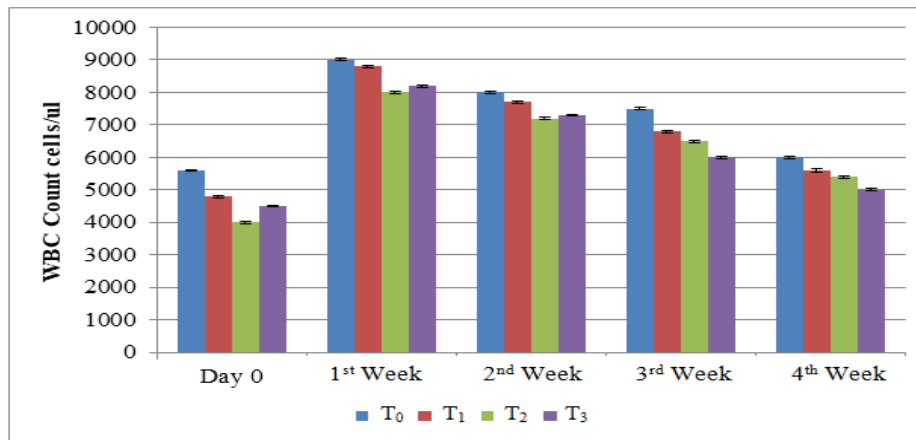
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**Table 3: Effects of turmeric extract, turmeric extract with ZnO nanoparticles and Bactrocin® on WBC count (cell/ul) of rabbit at weekly interval**

Treatment	Day 0	1 <sup>st</sup> week	2 <sup>nd</sup> week	3 <sup>rd</sup> week	4 <sup>th</sup> week
T <sub>0</sub>	5600±31.06 <sup>d</sup>	9000±36.47 <sup>d</sup>	8000±38.41 <sup>c</sup>	7500±36.11 <sup>d</sup>	6000±43.11 <sup>d</sup>
T <sub>1</sub>	4800±36.44 <sup>c</sup>	8800±39.41 <sup>c</sup>	7700±39.21 <sup>b</sup>	6800±37.32 <sup>c</sup>	5600±39.45 <sup>c</sup>
T <sub>2</sub>	4000±39.14 <sup>a</sup>	8000±40.11 <sup>a</sup>	7200±41.22 <sup>a</sup>	6500±32.44 <sup>b</sup>	5400±38.33 <sup>b</sup>
T <sub>3</sub>	4500±34.36 <sup>a</sup>	8200±35.21 <sup>a</sup>	7300±32.41 <sup>a</sup>	6000±37.22 <sup>a</sup>	5000±34.33 <sup>a</sup>
P-Value	0.000***	0.000***	0.000***	0.000***	0.000***

\*\*\* Significant at 1% level, Mean for wound recover size with different superscript within the rows were significantly different at p<0.01.

Here, T<sub>0</sub>= Control/non-treated group, T<sub>1</sub>= Hot iron burned and treated with turmeric extract, T<sub>2</sub>= Hot iron burned and treated with turmeric extract and ZnO-NPs, T<sub>3</sub>= Hot iron burned and treated with Bactrocin®



**Figure 3: Effects of turmeric extract, turmeric extract with ZnO nanoparticles and Bactrocin® on WBC count (cell/ul) of rabbit at weekly interval**

Comment [Ma12]: Please explain and state "Figure 3" in the main text

Here, T<sub>0</sub>= Control/non-treated group, T<sub>1</sub>= Hot iron burned and treated with turmeric extract, T<sub>2</sub>= Hot iron burned and treated with turmeric extract and ZnO-NPs, T<sub>3</sub>= Hot iron burned and treated with Bactrocin®

#### 4. CONCLUSIONS

The results of the study showed that that applying ZnO nanoparticles and turmeric extract to burn wounds in rabbits resulted in quicker wound healing with a shorter recovery period, demonstrating that treating burn wounds without the use of antibiotics is both feasible and advised.

Comment [Ma13]: Add few sentences factors that lead to quick recovery based from the results

#### REFERENCES (Please add more recent references, 5 years back)

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