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**Original Research**

# A clinical safety study of Kerra formula capsules following oral administration in healthy volunteers

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**Abstract**

**Background:** Kerra formula, derived from Tak-Ka-Si-La, an ancient Thai compilation, is composed of nine medicinal plants and used for its fever-reducing properties. It has been primarily employed to alleviate fever and was also used by some individuals in Thailand during COVID-19 infections. Moreover, a previous in vitro study indicated the potential of the Kerra formula to inhibit SARS-CoV-2 main protease and RNA-dependent RNA polymerase (RdRp). This study aimed to assess the safety and short-term side effects of Kerra formula capsules on 11 healthy volunteers. **Methods:** Two capsules of 500 mg were taken orally 4 times daily for 2 weeks. Symptoms, medical history, physical examination, and laboratory tests were examined. Parameters assessed included complete blood count, coagulation profiles, liver and renal function tests, urinalysis, inflammation markers, fasting blood sugar, and lipid profiles. **Results:** Comparing baseline and post-capsule results at 1, 7, and 14 days, and after a 14-day washout period, no abnormalities were found in physical examination. Moreover, no adverse reactions or statistically significant differences occurred in laboratory results. Additionally, favorable trends in blood pressure and lipid profiles suggest potential cardiovascular benefits. **Conclusion:** The study concludes that this protocol resulted in no deleterious effect in all volunteers, suggesting safe administration. However, further research is crucial to assess the herb's long-term effects. In particular, its potential role in preventing or mitigating COVID-19 infection should be investigated for safety through studies in animal models, followed by clinical research in infected individuals to establish therapeutic relevance and elucidate mechanisms of action.

**Keywords:** Kerra formula; Ancient Thai compilation; Safety Assessment; Oral Administration; Healthy Volunteers

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## INTRODUCTION

Thai traditional medicine, part of Thailand's cultural heritage and knowledge, is a holistic approach to treating and preventing disease in prehistoric times. Its holistic aspect emphasizes a healthy lifestyle, disease prevention, and health promotion. For example, Ka-min-chan (*Curcuma longa*) and Fa-tha-lai-jon (*Andrographis paniculata*) are Thai traditional herbal medicine which has been used as an alternative treatment for diseases, especially during epidemics[1,2]. They are practiced in Thailand as part of essential self-treatment remedies because it is believed to have anti-inflammatory and antioxidant properties. Recently, reports suggest that Fa-tha-lai-jon inhibits viral replication of SARS-CoV-2, thereby encouraging its use in the treatment of COVID-19[3]. The Ministry of Public Health of Thailand has approved its extract for COVID-19 treatment[4]. Kerra capsules are another traditional Thai herbal remedy reported to inhibit the activity of two SARS-CoV-2 enzymes, a main protease and an RNA-dependent RNA polymerase (RdRp)[5]. During the severe COVID-19 outbreak in Thailand, there has been a report of the use of the Kerra in patient care and for fever reduction[6,7].

Kerra capsule is a traditional Thai herbal remedy taken from the Taksila texts in the Royal Medical Manual of King Rama V. The recipes for Kerra capsules include a combination of various herbs, specifically nine medicinal plants. These include the heartwood of *Dracaena loureiri* Gagnep., the rhizomes of *Schumannianthus dichotomus* (Roxb.) Gagnep., the roots of *Citrus aurantifolia*, the roots of *Tiliacora triandra* (Colebr.) Diels, and *Tinospora crispa* (L.) Hook. f. & Thomson, the heartwood of *Tarenna hoaensis* Pit., the roots of *Momordica cochinchinensis* (Lour.) Spreng., the roots of *Combretum quadrangulare* Kurz. and the roots of *Dregea volubilis* (L.f.) Benth. ex Hook.f.[5]. In a 90-gram formulation, the composition includes *D. loureiri*, *T. crispa*, *S. dichotomus*, and *T. hoaensis*, at 10 grams each, together with the remaining herbal components. Kerra capsules are legally registered as a traditional medicine prescription, registration number G40/57, with the Food and Drug Administration (FDA), Department of Public Health, for treating fever. The trade name is Kerra Capsules, and manufactured by Vetchakorn Osot, Thailand. The herbal medicine appears as a brown powder packaged in capsules, with a content of 500 mg per capsule. The recommended dose is to take 1–2 capsules four times daily, before meals and before bedtime. The manufacturing facility adheres to Current Good Manufacturing Practice (cGMP) and International Organization for Standardization (ISO) 9001 certification standards to ensure quality and production control.

A study by Seetaha et al. (2022) using LC–MS/MS identified 414 annotated phytochemicals in the Kerra formula[5].Among them, three major compounds were identified, including 2-methoxy-9H-xanthen-9-one, isorhapontigenin, and betaine[5]. This study highlighted 2-methoxy-9H-xanthen-9-one as a prominent xanthone with diverse biological activities[8]. Isorhapontigenin is known for its anti-inflammatory and antiviral activities against SARS-CoV-2-infected Vero cells, while betaine exhibits anti-inflammatory effects by targeting NF-κB and NLRP3 signaling pathways[9,10]. These findings demonstrate the potential of Kerra as a natural source of anti-inflammatory and antiviral agents.

Although Kerra capsules have been reported regarding efficacy and pharmacological activity, no clinical trials have evaluated their safety in humans, leaving a gap in understanding potential risks and side effects. Therefore, this research was conducted to test the use and safety of the Kerra herbal formulation in healthy volunteers. The purpose of the research is to study the acute toxic effects of Kerra capsules on liver function, renal function, and blood system effects in healthy volunteers and the potential side effects of Kerra herbal formulation in healthy individuals. The anticipated benefits of the research are to gather information regarding the safety of consuming the Kerra capsules. These findings will serve as a foundation for future safety studies exploring the potential use of Kerra capsules in the prevention or mitigation of COVID-19 infection.

## METHODS

### Study design

This clinical safety study of Kerra capsules involved healthy volunteers from Nakhon Si Thammarat and surrounding provinces, who participated in the research project at Walailak University Medical Center Hospital, located at Walailak University in Nakhon Si Thammarat province, Thailand.

### Study population

Healthy volunteers aged 20-35 years who were described as capable of understanding the research methodology, making their own decisions, and signing an informed consent form to participate in the project participated in this study.

### Inclusion criteria

The inclusion criteria were healthy volunteers (male and female) aged 20 to 35 years with no congenital diseases, non-smokers, not regularly drinking alcohol or addicted to drugs, not regularly taking medications, supplements, or health maintenance products, with no history of coronavirus-2019 infection, and who gave informed consent to participate in the project.

### Exclusion criteria

Healthy volunteers who were unable to provide blood samples and had a history of allergies to medications, herbs, or foods. Pregnant volunteers or those who may become pregnant while participating in the research program. The volunteers were infected with COVID while participating in the project. The volunteers had abnormal laboratory results for their liver, kidney, coagulation levels, blood glucose, and anemia.

### Withdrawal criteria

The volunteers had symptoms indicative of Kerra capsules allergy or side effects, such as rash and frequent loose stools. Volunteers with abnormal laboratory results such as liver function tests (LFTs), renal function tests (RFTs), blood count, etc., such as AST, ALT increased three times, and creatinine increased more than 0.3. Volunteers experienced severe adverse events of level 3, which caused an inability to perform daily activities or caused an adverse reaction of level 3 or higher. Volunteers experienced both physical and mental illness during the study period. Volunteers did not follow the research proj-

ect procedures, which significantly affected the interpretation of the data. The volunteers were pregnant. The volunteers wish to withdraw from participation in the study.

**Sample size**

In this study, a random sample was drawn using purposive sampling, and the sample size was determined using the G*Power formula. The study deemed a total of 11 samples for statistical analysis[11]. The calculated 30 percent increased the sample; the number of volunteers in the sample was 14 because if some volunteers chose to stop participating during the study, the number of volunteers was still sufficient for statistical analysis.

**Intervention and outcomes**

The primary outcome was to evaluate the safety and tolerability of the Kerra formula by monitoring adverse events, physical examination findings, and key laboratory safety parameters. These parameters included complete blood count (CBC) to detect hematotoxicity, liver function tests (LFTs) to assess hepatotoxicity, renal function tests (RFTs) using blood urea nitrogen (BUN) and creatinine together with urinalysis to identify potential nephrotoxicity, coagulation tests to evaluate possible effects on the clotting system, and inflammatory markers such as Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) to detect systemic inflammation.

Secondary outcomes included time-dependent changes in fasting blood sugar (FBS), lipid profiles, and exploratory cardiovascular indicators such as blood pressure and lipid trends. Together, these biomarkers provide essential information for evaluating the short-term safety of herbal medicine use.

Healthy volunteers who met the inclusion criteria were given the herbal capsule (Kerra), a traditional medicine formulation with a registration number (G40/57). The dosage and intake period followed the requirements specified for the registered Kerra capsule formulation. Volunteers took two capsules (500 mg per capsule) four times per day, before breakfast, lunch, dinner, and bedtime, for 14 days. During the study, participants were prohibited from taking other medications or products.

The volunteers underwent a thorough physical examination conducted by a physician, encompassing measurements of height, weight, body temperature, blood pressure, pulse rate, respiratory rate, and blood oxygen saturation. In addition, assessments were performed on general characteristics and specific areas such as the head, neck, ears, nose, heart, lungs, abdomen, and nervous system. The examination also involved checking for any signs of allergies, including skin reactions or other allergic manifestations. Blood samples were collected on specific days in accordance with the Phase 1 protocol for the safety study of oral Triphala aqueous extract capsules in healthy volunteers. The collection schedule included days 1, 7, and 14 during the capsule regimen period and 14 days after completing the regimen[12]. During the examination, the physicians assessed the volunteers' vital signs, including their blood pressure, weight, height, and other relevant parameters.

For laboratory testing, blood was drawn into tubes containing 3.2% sodium citrate as an anticoagulant, as well as tubes without anticoagulant and tubes containing anticoagulants such as ethylenediaminetetraacetic acid (EDTA) and sodium fluoride (NaF). Random urine samples were also collected for analysis. The blood samples collected in EDTA anticoagulant tubes were used for CBC analysis, while the samples collected in 3.2% sodium citrate anticoagulant tubes were used for coagulation factor analysis. Coagulation assays were conducted using the plasma samples, including prothrombin time (PT) and activated partial thromboplastin time (aPTT). Liver function was assessed by measuring levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT),and alkaline phosphatase (ALP), while renal function was evaluated by measuring BUN and serum creatinine. The serum lipid profile was determined. Inflammation was assessed using the ESR assay from EDTA blood samples, and serum CRP levels were measured. FBS was tested from plasma samples collected in NaF tubes. Urinalysis was performed to assess kidney function.

**Adverse event**

While the volunteers were taking the Kerra capsules, the researcher continuously monitored the volunteers' symptoms for adverse reactions after 1 day, 7 days, 14 days after taking the Kerra capsules, and 14 days after stopping taking the Kerra capsules; any adverse events and side effects experienced by the volunteers were carefully recorded in a designated form. The side effects were observed and analyzed throughout the period of taking the Kerra capsules.

**Data analysis**

Descriptive statistics were used to present the frequency, percentage, mean, standard deviation, median, and quartile range in explaining the general information and side effects or symptoms noted while taking the Kerra capsules. Analysis of covariance (ANCOVA) analysis was used to compare laboratory results with repeated measures. If the results were significantly different (P value < 0.05), then the next pairwise analysis (post-hoc test) was performed using the Bonferroni method. For variables with abnormal distribution characteristics, statistics in groups were used nonparametrically. Friedman test and next pairs were used to compare by Wilcoxon Signed Ranks test statistics. Partial eta-squared ($\eta^2$) was included to quantify the magnitude of within-subject changes, with thresholds interpreted as small effect (≥0.01), medium effect (≥0.06), and large effect (≥0.14) [13].

## RESULTS

**Healthy volunteers**

A total of 24 volunteers, including 11 men and 13 women, participated in health assessment by history taking, physical examination, and laboratory testing by physicians. A total of nineteen healthy volunteers, comprising 10 women and 9 men, were randomly assigned into two groups: 7 men and 7 women. These groups were selected to take the Kerra capsules as part of the study. During the study, three volunteers had to be withdrawn from participation. One volunteer decided to withdraw their consent to continue in the study, another volunteer was

taking another drug concurrently, and one volunteer was infected with coronavirus-2019 (COVID-19). Therefore, the study included a total of 11 healthy volunteers who participated and provided complete research data. Among these volunteers, there were 5 women and 6 men, with ages ranging from 20 to 33 years (Figure 1).

**Results of the physical examination**

The physical examination results of the volunteers indicated normal findings with no evidence of adverse effects. A covariance test was conducted to analyze repeated measurements of BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), body temperature (BT), pulse rate (PR), respiratory rate (RR), and blood oxygen saturation ($SpO_2$) are shown in Table 1. The analysis revealed no statistically significant differences in SBP values at any of the assessed time points, including the baseline before taking the Kerra capsules and at 1, 7, and 14 days after intake and after a 14-day washout period (P = 0.548). The effect size (partial $\eta^2$) indicated a 7.9% effect on SBP. Similarly, DBP values did not exhibit significant variations across different time points (P = 0.966), with the effect size (partial $\eta^2$) suggesting a 1.5% effect on DBP (Table 1).

Additionally, no significant differences were observed in BMI at the assessed time points, including before taking the Kerra capsules, as well as at 1, 7, and 14 days after taking the Kerra capsules, and after a 14-day washout period (P=0.585). The effect size (partial $\eta^2$) indicated a 7.4% effect on BMI. Furthermore, parameters such as BT, PR, RR, $SpO_2$ showed no significant differences (P > 0.05) (Table 1).

**Complete blood count and blood coagulation profiles**

The results of the CBC test conducted before and after taking the Kerra capsules for 1, 7, and 14 days, and after a 14-day washout period, are shown in Table 2.

The CBC results, which encompassed measurements of hemoglobin, hematocrit, erythrocyte count, red blood cell indices (MCV, MCH, MCHC), RDW, white blood cell count, and the percentages of neutrophils, lymphocytes, monocytes, eosinophils, basophils, and platelet count, did not exhibit statistically significant changes at 1, 7, and 14 days after taking the Kerra capsules, as well as 14 days after discontinuing the Kerra capsules, in comparison to the baseline values prior to taking the capsules. When considering the influencing variable (Partial $\eta^2$), it indicated that the effect of Kerra capsules on various blood parameters was as follows: there was a 1.2% change in hemoglobin, a 0.9% change in hematocrit, a 2.0% change in erythrocyte count, a 7.1% change in MCV, a 5.6% change in MCH, an 11.5% change in MCHC, a 7.4% change in RDW, an 8.7% change in neutrophils, a 6.5% change in lymphocytes, a 6.0% change in monocytes, and a 21.1% change in eosinophils (Table 2).

The results of coagulation tests in the pre-intervention period, during the intake of the Kerra capsules for 1, 7, and 14 days, and after a 14-day washout period are presented in Table 2.

No statistically significant changes were observed in PT values (P = 0.858), with mean values within the normal range. The effect size (Partial $\eta^2$) indicated a 1.1% effect of the Kerra capsule formulation on PT. Similarly, aPTT values showed no statistically significant changes (P = 0.258), with mean values within the normal reference range. The effect size (Partial $\eta^2$) suggested a 13.9% effect of the Kerra capsules on aPTT (Table 2).

**Blood chemistry parameters and inflammation assessments**

The results of liver function tests, renal function tests, lipid profiles, FBS levels, and inflammation tests at baseline values, as well as at 1, 7, and 14 days after taking the Kerra capsules and following a 14-day washout period, are displayed in Table 3.

Liver function was assessed by measuring AST, ALT, and ALP values during the pre-study period, the intake of Kerra capsules, and the washout period. The mean values of AST, ALT, and ALP were compared across the pre-intervention, Kerra capsule intake, and washout periods. No statistically significant differences were observed between these time points (P > 0.05).The mean values of AST, ALT, and ALP remained within the normal range throughout the Kerra capsule intake and follow-up period. When considering the effect size, it was found that the Kerra capsule had a Partial $\eta^2$ value indicating an effect of 14.5% on AST, 20.1% on ALT, and 5.7% on ALP (Table 3).

Renal function was assessed by measuring BUN and creatinine levels during the pre-study period, the intake of Kerra capsules, and the washout period. After taking the Kerra capsules, there were no statistically significant changes in BUN and creatinine levels compared to the pre-intervention period (P > 0.05). The mean value of BUN during the period of taking the capsules and the follow-up periods remained within the normal range. When the effect size was considered, it was found to have Partial $\eta^2$= 0.033, which indicated that Kerra capsules had an effect of 3.3% on BUN and 12.4% on creatinine. Moreover, there was no evidence of abnormality in the urinalysis results (Table 3).

The lipid profiles, which include total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels, were assessed during the pre-study period, the intake of Kerra capsules and the washout period. No statistically significant changes were observed in these parameters (P > 0.05). However, when considering the effect size, the Kerra capsule formulation showed an effect of 6.6% on cholesterol, 6.5% on triglycerides, 17.0% on HDL-C, and 6.0% on LDL-C, as indicated by the Partial $\eta^2$ value.

The blood sugar (FBS) levels were assessed before the intervention, after taking the Kerra capsules, and during the washout period. There were no significant differences in FBS values observed. However, the effect size analysis revealed that the Kerra capsules had a Partial $\eta^2$ value of 0.055, indicating a 5.5% effect on FBS. The mean FBS values in all-time points remained within the normal range (Table 3).

The inflammation tests were conducted during the pre-intervention period, the intake of the Kerra capsules, and the washout period. The median values of ESR and CRP showed no statistically significant changes compared to the baseline values (P = 0.603 and P = 0.878, respectively) (Table 3).

## DISCUSSION

The present study aimed to investigate the safety of Kerra capsules, a traditional medicine preparation derived from the Book of Taksila. The study's results demonstrated that administering Kerra capsules at the prescribed dosage and duration did not elicit any adverse reactions in the healthy volunteers.

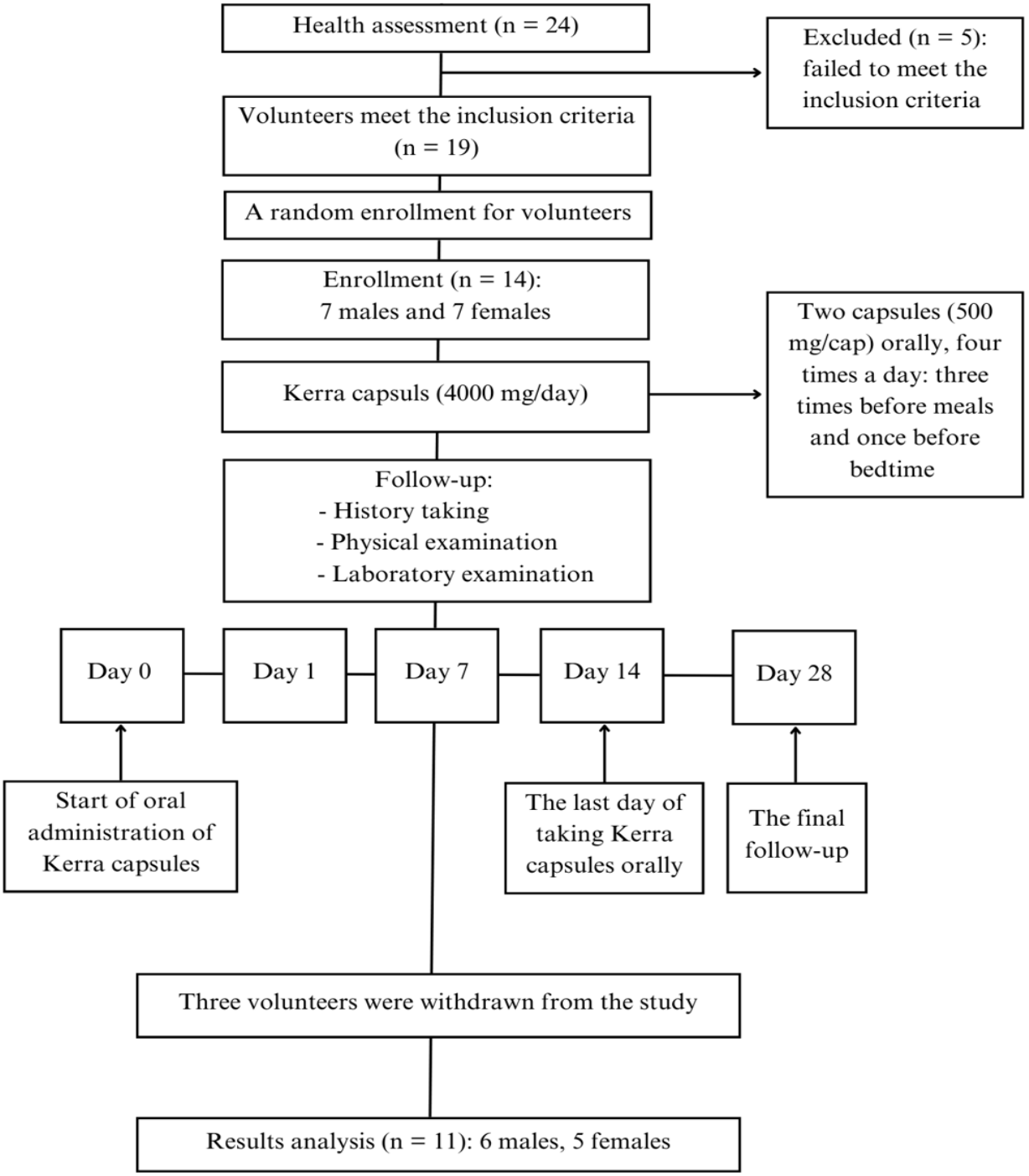


**Figure 1.** The flowchart illustrating the trial process


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**Table 1.** Physical examination findings of healthy volunteers taking Kerra capsules.

| Parameter | Baseline | Treatment period | | | Follow-up after 14 days | Partial $\eta^2$ | P-value |
|---|---|---|---|---|---|---|---|
| | | 1 day | 7 days | 14 days | | | |
| BT (35.4 – 37.4 °C) | 36.75 ± 0.20 | 36.31±0.91 | 36.65 ± 0.19 | 36.69 ± 0.20 | 36.74 ± 0.31 | 0.193 | 0.164 |
| BMI (18.5 – 24.9 kg/m$^2$) | 22.01 ± 3.22 | 21.82 ± 3.13 | 21.89 ± 3.27 | 21.89 ± 3.29 | 21.79 ± 3.12 | 0.074 | 0.585 |
| SBP (120-129 mmHg) | 125.45 ± 10.92 | 119.55 ± 10.48 | 120.09 ± 15.37 | 117.64 ± 14.43 | 110.36 ± 15.87 | 0.079 | 0.548 |
| DBP (80 – 84 mmHg) | 73.55 ± 10.13 | 72.73 ± 7.56 | 73.27 ± 8.88 | 69.00 ± 10.00 | 69.45 ± 7.70 | 0.015 | 0.966 |
| PR (60 – 100 bpm) | 81.09 ± 12.69 | 76.18 ± 10.22 | 80.82 ± 15.64 | 81.45 ± 11.76 | 77.09 ± 9.31 | 0.056 | 0.713 |
| RR (20 – 26 bpm) | 20.00 ± 0.00 | 20.00 ± 0.00 | 20.00 ± 0.00 | 20.00 ± 0.00 | 20.18 ± 0.60 | 0.133 | 0.269 |
| $SpO_2$ (96 – 100 %) | 98.91 ± 0.83 | 99.36 ± 1.12 | 98.09 ± 1.04 | 98.55 ± 0.93 | 99.28 ± 0.90 | 0.12 | 0.12 |

**BT:** body temperature; **BMI:** body mass index; **SBP:** systolic blood pressure; **DBP:** Diastolic blood pressure; **PR:** pulse rate; **RR:** Respiratory rate; **$SpO_2$:** oxygen saturation.

Data were analyzed using One-way repeated measure ANCOVA (Analysis of Covariance).

Physical examinations and laboratory tests conducted before and after the consumption of Kerra capsules revealed no abnormalities or significant differences, suggesting the absence of any negative effects on the participants' overall health. Interestingly, systolic and diastolic blood pressure showed a slight downward trend, suggesting a potential benefit of Kerra formula in supporting cardiovascular health. These findings support the notion that Kerra capsules can be safely administered to healthy individuals.

Regarding the main ingredients of Kerra herbs, which include the nine herbal components mentioned earlier, previous studies on the safety of individual medicinal plants have reported the following findings. *Dracaena loureiri* Gagnep. demonstrated no acute toxicity to mice and chronic toxicity to rabbits[14]. *Schumannianthus dichotomus* (Roxb.) Gagnep. exhibited no acute toxicity in mice[15]. Root of *Citrus aurantifolia* displayed no acute or subacute toxicity in rats[16]. *Tiliacora triandra* (Colebr.) Diels demonstrated no acute and subchronic toxicity in mice[17]. *Tinospora crispa* (L.) Hook. f. & Thomson exhibited no acute toxicity but indicated chronic toxicity to the liver and kidneys in mice[18]. Notably, liver toxicity has been reported in humans who consumed *Tinospora crispa* for six months[19]. However, no scientific reports have been published on the acute or chronic toxicity of the heartwood of *Tarenna hoaensis* Pit., the roots of *Momordica cochinchinensis* (Lour.) Spreng., *Combretum quadrangulare* Kurz. and, *Dregea volubilis* (L.f.) Benth. ex Hook.f. These findings suggest the importance of assessing the safety of the entire herbal formulation, such as Kerra capsules, rather than focusing solely on individual components. In terms of their pharmacological mechanisms, the nine herbal components in Kerra may interact synergistically, as their phenolic, flavonoid, alkaloid, and glycoside constituents could work together to enhance antiviral activity and reinforce anti-inflammatory effects, creating a broader and more balanced biological response than any single herb alone[5].

In 2021, the Toxicology Laboratory of Medical Plant Research Institute, Department of Medical Sciences, Thailand (2021), conducted acute toxicity testing of herbal recipes (Kerra capsules) on mice. The study followed OECD standards from 2001 and administered Kerra powder suspended in distilled water at 0.125 g/ml concentration to oral test mice. The mice were orally administered a dose of 20 ml per kg body weight twice with a 4-hour interval. It was observed that the rats given the herbal formula (Kerra capsules) did not exhibit any abnormal symptoms during the testing period. All rats survived, and no pathological visceral abnormalities were observed when compared to the control group. These findings indicate that the herbal medicine (Kerra capsules) has very low acute toxicity. The LD50 value, representing the lethal dose to 50% of the sample population, was found to be greater than 5 g/kg, classifying it under Category 5. These findings further support and reinforce the safety profile of the capsules.

The effects of the Kerra capsules on the hematopoietic system were evaluated through a complete blood count, which assesses the quantity and quality of blood cells, including red blood cells, white blood cells, and platelets. Herb-induced poisoning can lead to reduced blood formation, increasing the risk of septicemia and infection[20]. Studies on the Kerra capsules have demonstrated no impact on all three types of blood cells, the total count of blood cells, and the percentage of each type of white blood cell. No significant differences were observed before and after taking the capsules, and the volunteers did not exhibit any signs of anemia.

Several herbal products have been reported to exhibit antiplatelet and/or anticoagulant properties, which can potentially interfere with the normal blood clotting process and increase the risk of bleeding[21]. For instance, Purple Loosestrife (*Lythrum salicaria* L.) has been found to prolong PT values[22]. Kelp (*Monostroma latissimum* (Keutzing) Wittrock) can also prolong aPTT values[23]. To evaluate Kerra's effect on blood coagulation, the function of coagulation factors was evaluated using coagulation tests, PT and aPTT. PT assesses the coagulation factors involved in the extrinsic pathway (X, V, II, and I), while aPTT evaluates coagulation factors in the intrinsic pathway (VIII, IX, XI, XII, prekallikrein, and high molecular weight kininogen) as

**Table 2.** Blood cell count and coagulation profiles of healthy volunteers taking Kerra capsules.

| Parameter | Baseline | Treatment period | | | Follow-up after 14 days | Partial $\eta^2$ | P-value |
|---|---|---|---|---|---|---|---|
| | | 1 day | 7 days | 14 days | | | |
| Hb (11.5 – 17.0 g/dL) | 13.90 ± 1.84 | 14.06 ± 1.73 | 13.98 ± 1.64 | 13.88 ± 1.69 | 14.02 ± 1.72 | 0.012 | 0.978 |
| Hct (37.0 – 54.0 %) | 41.05 ± 5.34 | 41.39 ± 5.06 | 41.40 ± 4.56 | 41.12 ± 4.45 | 41.45 ± 4.63 | 0.009 | 0.987 |
| RBC (3.75 – 6.54 x$10^6$/µL) | 4.84 ± 0.60 | 4.87 ± 0.61 | 4.87 ± 0.56 | 4.83 ± 0.58 | 4.87 ± 0.58 | 0.02 | 0.946 |
| MCV (80.0 – 100.0 fL) | 84.89 ± 3.95 | 85.19 ± 3.99 | 85.11 ± 3.98 | 84.73 ± 3.88 | 85.22 ± 3.92 | 0.071 | 0.495 |
| MCH (27.0 – 32.0 pg) | 28.21 ± 2.21 | 28.89 ± 1.20 | 28.72 ± 1.17 | 28.76 ± 1.13 | 28.77 ± 1.14 | 0.056 | 0.493 |
| MCHC (32.0 – 36.0 g/dL) | 33.92 ± 1.02 | 33.94 ± 0.96 | 33.75 ± 0.95 | 33.47 ± 2.42 | 33.81 ± 1.00 | 0.115 | 0.315 |
| RDW (11.0 – 16.0 %) | 12.89 ± 0.79 | 12.81 ± 0.83 | 12.75 ± 0.74 | 12.66 ± 0.74 | 12.69 ± 0.81 | 0.074 | 0.584 |
| WBC (4,000 – 10,000 cells/µL), median (IQR)† | 6,520(5,810 – 7,340) | 6,630(5,510 – 6,860) | 6,780(6,210 – 7,630) | 6,560(5,780 – 6,950) | 6,550 (6,150 – 7,010) | - | 0.116 |
| Neu (40 – 75 %) | 48.82 ± 9.57 | 47.09 ± 9.82 | 50.64 ± 8.80 | 51.27 ± 5.71 | 49.27 ± 9.45 | 0.087 | 0.499 |
| Lym (20 – 45 %) | 40.27 ± 8.30 | 41.82 ± 8.80 | 37.91 ± 6.88 | 38.27 ± 5.59 | 40.18 ± 9.93 | 0.065 | 0.647 |
| Mono (2 – 10 %) | 6.82 ± 1.08 | 7.09 ± 1.04 | 6.91 ± 1.45 | 6.82 ± 1.47 | 6.09 ± 1.64 | 0.06 | 0.683 |
| Eos (0 – 6 %) | 3.55 ± 2.12 | 3.64 ± 1.43 | 3.18 ± 1.54 | 3.27 ± 1.62 | 3.73 ± 2.41 | 0.211 | 0.106 |
| Bas (0 – 1 %), median (IQR)† | 1 (0, 1) | 0 (0, 1) | 1 (0, 1) | 0 (0, 1) | 0 (0, 1) | - | 0.8 |
| Plt (140 – 400x$10^3$/µL),median (IQR)† | 272 (249, 308) | 280 (228, 300) | 266 (235, 306) | 271 (233, 330) | 257 (239, 341) | - | 0.97 |
| PT (13.0 – 15.0 sec) | 11·84 ± 0·32 | 11·73 ± 0·58 | 11·91 ± 0·45 | 12·78 ± 1·27 | 12·01 ± 0·57 | 0·011 | 0·858 |
| aPTT (25.0 – 43.0 sec) | 26·47 ± 3·46 | 26·76 ± 2·22 | 25·96 ± 2·72 | 26·43 ± 1·99 | 26·31 ± 2·34 | 0·139 | 0·258 |

**Hb:** hemoglobin; **Hct:** Hematocrit; **RBC:** red blood cell count, **MCV:** mean corpuscular volume; **MCH:** mean corpuscular hemoglobin: **MCHC:** Mean corpuscular haemoglobin concentration; **WBC:** white blood cells; **Neu:** neutrophils; **Lym:** lymphocytes; **Mono:** monocytes; **Eos:** eosinophils; **Bas:** basophils; **Plt:** platelet count; **PT:** prothrombin time, **aPTT:** activated partial thromboplastin time.
Data were analyzed using One-way repeated measure ANCOVA (Analysis of Covariance) and the Friedman test†

well as the common pathway. In the case of Kerra capsules, no inhibitory effects on blood clotting factors were observed. The coagulation values, including PT and aPTT, remained within the normal range, with no significant difference observed before and after taking the Kerra capsules.

Previous studies have indicated that certain herbs can be hepatotoxic and result in increased detection of liver enzymes in the blood, such as *Morinda citrifolia*[24,25]. The hepatotoxicity assessment involving liver enzymes, including AST, ALT, and ALP, in the blood samples revealed the laboratory results within the normal range during the Kerra capsule consumption and for 14 days after discontinuation of the medication. This result indicated that Kerra capsules do not induce acute hepatotoxicity.

The kidney is susceptible to toxic substances, including drugs, which can result in acute kidney injury. Medicinal plants have been associated with various kidney diseases, including tubular necrosis, acute interstitial nephritis, chronic interstitial nephritis, nephrolithiasis, urinary retention, and urinary tract cancer[26]. In the assessment of the Kerra capsules' nephrotoxicity, BUN and creatinine levels were examined. The study revealed that BUN and creatinine values remained within the normal range, showing no significant increase. Additionally, urine test results were within the normal range, indicating the absence of acute nephrotoxicity.

The analysis of FBS levels showed no significant changes following the consumption of Kerra capsules, indicating that the capsules did not disrupt the normal regulation of blood glucose. Moreover, there was no evidence of inflammation, as indicated by ESR and CRP levels, suggesting that the Kerra capsules did not induce inflammatory conditions in the body.

Although no statistically significant differences were observed across these physiological and laboratory parameters, the partial eta-squared values, reflecting how strongly the treatment or time influences changes in measurements, suggested minor

**Table 3.** Blood chemistry, erythrocyte sedimentation rate, and C-reactive protein of healthy volunteers taking Kerra capsules.

| Parameter | Baseline | Treatment period | | | Follow-up after 14 days | Partial $\eta^2$ | P-value |
|---|---|---|---|---|---|---|---|
| | | 1 day | 7 days | 14 days | | | |
| AST (0 – 40 U/L) | 20.00 ± 5.14 | 19.27 ± 4.45 | 19.09 ± 4.64 | 20.64 ± 7.17 | 20.18 ± 4.40 | 0.145 | 0.214 |
| ALT (0 – 50 U/L) | 14.64 ± 8.41 | 14.82 ± 6.82 | 14.73 ± 6.33 | 17.09 ± 11.50 | 14.64 ± 6.62 | 0.201 | 0.142 |
| ALP (40 – 129 U/L) | 65.18 ± 14.39 | 60.00 ± 22.15 | 65.91 ± 14.18 | 63.45 ± 14.23 | 64.36 ± 13.63 | 0.057 | 0.516 |
| BUN (6 – 20 mg/dL) | 10.5 ± 2.81 | 10.09 ± 2.51 | 12.36 ± 4.93 | 11.55 ± 1.64 | 12.27 ± 1.90 | 0.033 | 0.846 |
| Crea (0.67 – 1.17 mg/dL) | 0.86 ± 0.22 | 0.84 ± 0.20 | 0.87 ± 0.17 | 0.85 ± 0.18 | 0.86 ± 0.20 | 0.124 | 0.299 |
| TC (0 – 200 mg/dL) | 195.73 ± 30.36 | 195.91 ± 25.97 | 194.18 ± 24.05 | 192.64 ± 28.81 | 191.18 ± 23.16 | 0.066 | 0.527 |
| Tg (0 – 150 mg/dL) | 83.73 ± 22.40 | 97.27 ± 21.13 | 94.18 ± 24.90 | 82.45 ± 17.85 | 98.09 ± 46.16 | 0.065 | 0.554 |
| HDL-C (> 55 mg/dL) | 65.73 ± 7.34 | 65.09 ± 6.83 | 66.73 ± 8.45 | 68.00 ± 9.24 | 65.45 ± 6.50 | 0.17 | 0.143 |
| LDL-C (0 – 100 mg/dL) | 128.00 ± 26.98 | 126.18 ± 24.06 | 124.73 ± 23.29 | 122.36 ± 26.48 | 120.64 ± 19.02 | 0.06 | 0.581 |
| FBS (74 – 99 mg/dL) | 88.64 ± 6.15 | 86.45 ± 5.17 | 88.64 ± 2.87 | 87.73 ± 4.59 | 89.09 ± 5.58 | 0.055 | 0.716 |
| ESR (0 – 20 mm/hr), median (IQR)† | 6 (5, 15) | 7 (5, 19) | 7 (5, 19) | 9 (5, 14) | 8 (5, 23) | - | 0.603 |
| CRP (0 – 5 mg/dL), median (IQR)† | <0.6 (<0.6, 1) | <0.6 (<0.6, 1) | <0.6 (<0.6, 1) | <0.6 (<0.6, 1) | <0.6 (<0.6, 1) | - | 0.878 |

**AST:** aspartate aminotransferase, **ALT:** alanine aminotransferase, **ALP:** alkaline phosphatase, **BUN:** blood urea nitrogen, Crea; creatinine, **FBS:** fasting blood sugar, **TC:** total cholesterol; **Tg:** triglyceride; **HDL-C:** high-density lipoprotein cholesterol; **LDL-C:** low-density lipoprotein cholesterol; **ESR:** erythrocyte sedimentation rate, **CRP:** C-reactive protein
Data were analyzed using One-way repeated measure ANCOVA (Analysis of Covariance) and the Friedman test†

variability over time. All results nevertheless remained within normal clinical ranges, supporting the short-term safety of Kerra capsules.

Additionally, the impact of the herbal medicine on blood lipid levels was assessed. The study examined total cholesterol, triglycerides, HDL-C, and LDL-C levels before and after taking the Kerra capsules. Although changes in lipid parameters were not statistically significant, lipid profiles remained stable throughout the intervention, supporting the short-term safety and metabolic neutrality of the Kerra formula. Despite participants having normal BMI, baseline LDL-C levels were slightly elevated, reflecting individual differences in lipid metabolism. Modest improvements were observed, including slight reductions in total cholesterol and LDL-C and a mild increase in HDL-C, while triglycerides returned to baseline by day 14. All values remained within acceptable clinical limits, suggesting no adverse effects and potential benefits for lipid regulation.

In order to guarantee the proper and safe use of herbal remedies, pharmacists play a critical role in ensuring the safe and appropriate use of herbal medicines. Identifying possible herb-drug interactions, assessing product quality and safety, and making sure herbal remedies are administered in accordance with evidence-based guidelines are some of their duties. In order to help patients make educated decisions, pharmacists also offer advice on appropriate use, anticipated advantages, potential side effects, and safety measures. These roles become more crucial to protect patient health and encourage the sensible use of traditional medicines in contemporary pharmacy practice as herbal products like the Kerra formulation become more widely used.

In both community pharmacies and hospital settings, these duties are directly related to day-to-day pharmacy practice. While clinical pharmacists play a crucial role in reviewing patients' use of herbal medicines, working with multidisciplinary teams, monitoring herb-drug interactions, and reporting or surveilling adverse events as part of pharmacovigilance systems, they are the initial point of contact for accurate information, advice on proper use, risk assessment, and monitoring for potential adverse effects.

The use of herbal products for immune support and prevention significantly increased during the COVID-19 pandemic. This increased the significance of pharmacists in the following areas: providing evidence-based information; preventing overuse or misuse; monitoring population-level risks related to the widespread use of herbal medicines; and supporting safety assessment within public health surveillance systems. Overall, this study emphasizes the incorporation of herbal medicine safety into modern pharmacy practice and reaffirms the critical role that pharmacists play in all practice settings. Increasing pharmacist proficiency in these areas will improve patient outcomes and raise the general safety of using herbal medicines in the medical system.

The study's limitations include the restricted volunteer group and setting, which may hinder the generalizability of the findings to wider populations or regions. Furthermore, the study lacks evaluation of the intervention's long-term effects, necessitating further research to assess its sustained effects over an extended duration.

## CONCLUSIONS

In conclusion, this clinical safety study in healthy volunteers provides valuable insights into the safety profile of the Kerra capsules as a traditional medicine formulation. The findings suggest that the capsules can be safely consumed at a dosage of 1,000 mg per dose, taken four times a day for 14 consecutive days, without adverse reactions or negative effects on various health parameters. However, it is essential to consider the potential long-term effects and conduct further research, particularly in populations with specific health conditions or individuals taking concomitant medications. Future research should investigate the potential of Kerra capsules to prevent or mitigate the severity of viral infections, such as COVID-19, through preclinical studies in animal models followed by clinical trials in human patients to establish safety and efficacy.

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## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Human Research Ethics Committee of Walailak University (certificate number WUEC-22-302-01). The Thai Clinical Trials Registry (TCTR) identification number is TCTR20230320009 (https://www.thaiclinicaltrials.org/show/TCTR20230320009).

## AUTHORS' CONTRIBUTIONS

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All authors have read and approved the final version of the manuscript.

## CONFLICTS OF INTEREST

Suriyan Sukati received support from EASTERN HERB CO., LTD., Nonthaburi, Thailand, which provided the herbal materials used in this study. The company had no role in study design, data collection, analysis, or manuscript preparation. All other authors have no conflicts of interests to declare.

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