Antimicrobial activity, toxicity and retrospective clinical effectiveness of Kantinka BA and Kantinka Herbaltics, two multi-component-herbal products used in the management of infectious diseases in Ghana

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Abstract

There is an upsurge in the incidence of persons living with infectious diseases and their associated symptoms. Also, there is increased resistance and high cost of available synthetic antimicrobial therapeutic agents. This calls for screening candidate herbal products to examine the risk-to-benefit ratio for users. Moreover, there are inadequate proven scientific studies to assess the quality, effectiveness, and toxicity of herbal products that traditional medicine practitioners in Ghana commonly use for the management of infectious diseases such as those caused by *Neisseria gonorrhoeae*, *Candida albicans* and the symptomatic management of symptoms associated with infections like cough, skin infections among others and gastritis. Kantinka BA and Kantinka Herbaltics, two multicomponent herbal products, have been used to manage the above-mentioned disease conditions. The study aims to evaluate the *in vitro* antibacterial activity, assess the retrospective clinical effectiveness (clinical responses; the disappearance of presenting signs and symptoms associated with infections, gastritis), and the quality and toxicity of Kantinka BA and Kantinka Herbaltics. The products are registered by the Food and Drugs Authority (FDA). Data on 200 patients who were diagnosed with infectious diseases such as Human Immunodeficiency Virus (HIV) / Acquired Immunodeficiency Syndrome (AIDS) and associated symptoms from January 2018 to June 2018 was obtained from the Adom Herbal Clinic, and the Tafo Government Herbal Medicine Records Unit was assessed. The antibacterial activity of the products was evaluated using the HT-SPOTi method. Phytochemical screening, microbial load, and pH were carried out according to standard procedures. Acute toxicity was carried out according to the Organization for Economic Cooperation and Development (OECD) guideline 425. Phytochemical screening, pH, and microbial load have been established for both products. Binding toxicity studies revealed that the products are non-toxic at a 2000 mg/kg dose. The two products exhibited antimicrobial activities against the test organisms with Minimum Inhibitory Concentration (MIC) and Minimum Lethal Concentration (MLC) determined for Kantinka BA and Kantinka Herbaltics as 5% and 10% and <80, respectively, against *C. albicans* and *N. gonorrhoeae* - the signs and symptoms associated with infections disappeared during the management period. The products are safe and may effectively manage some infectious diseases and associated symptoms.

Introduction

Medicinal plants and products have always been the most widespread form of therapy in humanity.[1-3] These products are generally used by patients suffering from chronic diseases such as diabetes, hypertension, stroke, infectious diseases, and their associated symptoms. This is usually due to the high costs and the mainly symptomatic treatment in conventional medicine. Patients with symptoms such as boils, skin infections, and coughs (usually immunocompromised) also prioritize using traditional medicine.[4]

Infections and infectious diseases affect people of all ages, from newborns to the elderly, and represent a significant reason for medical consultation.[5] Skin diseases, coughs, and diarrhea are a considerable concern due, among other things, to their association with other infectious diseases and conditions. The World Health Organization (WHO) states that contagious diseases contribute significantly to the cause of morbidity and mortality worldwide, accounting for approximately 50% of all deaths, particularly in the tropical regions of the world.[6] Antimicrobial resistance has become one of the greatest threats to public health and poses serious problems for successfully preventing and treating persistent diseases.[7] These are an ever-increasing spectrum of infections caused by various organisms such as bacteria, parasites, viruses, and fungi. Most pathogens are no longer susceptible to the common medications used to treat them. This has resulted in significant human suffering and enormous economic losses.[8,9] Although allopathic drugs are used and have proven helpful in the treatment of microbial infections, factors such as inappropriate use of antibiotics in patients, increase in secondary infections, cost, and adverse drug reactions[10] justify the search for alternative agents. Furthermore, the extensive use of antibiotics in the animal industry has resulted in intense selection pressure for the emergence of antibiotic-resistant bacteria, thus leading to a strong resurgence in the use of herbal products.[11,12] Furthermore, increasing patient mobility and travel worldwide have led to increased transmission of drug-resistant organisms from one country to another.[13] These factors observed in widespread antibiotic resistance pose a severe challenge to public health, leading to the search, use, and marketing of herbal products known to possess antimicrobial activity. This is because herbal products are considered safe, effective, culturally acceptable, affordable, and unlikely to cause antimicrobial resistance.[14] In Ghana, the use of herbal medicine is a common practice in both rural and urban areas. Herbal medicine services have been integrated into Ghana's health care delivery system since 2011, and there is a Recommended Herbal Medicines List (RHML) developed by the Ministry of Health. The RHML contains selected herbal products for Herbal Medicine Practitioners (HMPs) at Herbal units in government hospitals to prescribe from. Two (2) of such herbal products are often defined by HMPs and have a long history of use for managing some infectious diseases and their symptoms, Kantinka BA and Kantinka Herbaltics.[15]

Kantinka BA and Kantinka Herbaltics have been developed as polyherbal products. They are prescribed to be taken together for the desired therapeutic actions. However, clinical data is needed to validate their effectiveness despite their frequent and long-term use. This has, therefore, necessitated the need to assess the toxicity, antimicrobial activity, and clinical potential of the two products in managing infectious diseases. The products have been duly registered with the Food and Drugs Authority (FDA), Ghana, since 2000. The medicinal plants constituents and their uses, and the indications of Kantinka BA and Kantinka Herbaltics are indicated in Table 1.[16-23]

Materials and Methods

Reagents, glassware, and instrumentation for quality assessment of Kantinka BA and Kantinka Herbaltics

Laboratory equipment, reagents and glassware including pH meter, concentrated HNO_3, concentrated HCl, H_2O, nutrient agar, MacConkey agar, Sabouraud agar, Salmonella agar, Shigella agar and potato dextrose agar, laboratory incubator (Gallenkamp; London, UK), oven (Gallenkamp), electric scales (Mettler Toledo; Columbus, USA) and general laboratory glassware were obtained from the central warehouses of the Department of Microbiology, Kwame Nkrumah University of Science and Technology (KNUST), Ghana.[24]

Test samples

The samples for the study, Kantinka BA and Kantinka Herbaltics, are finished herbal products manufactured by Adom Herbal Clinic and Products, Tema, Ghana. About ten samples from three different batches were selected for research purposes. They were obtained from the Herbal Medicine Unit (HMU) of Tafo Government Hospital, Kumasi, Ghana.

Phytochemical screening

The different batches of samples were qualitatively screened for the presence of secondary metabolites including alkaloids, terpenoids, flavonoids, phytosterols, anthraquinones, saponins, tannins and glycosides following standard procedures.[25,26]

Microbial load determination

The microbial load analysis for Kantinka BA and Kantinka Herbaltics was determined using nutrient agar, MacConkey agar, Sabouraud agar, Salmonella agar, Shigella agar, and potato dextrose agar according to standard methods.[27] The microbial content of Kantinka BA and Kantinka Herbaltics was analyzed at the

Table 1. Medicinal plants constituents, their uses and indication of Kantinka BA and Kantinka Herbaltics.

Herbal product	Constituents	Uses	Indication of herbal product
Kantinka BA	*Piper umbellatum*	Skin and gastric disorders[16] and anti-bacterial[17]	Sexually Transmitted Diseases (STDs), boils, and skin rashes.
	Vernonia conferta	Venereal diseases and stomach disorders[18]	
	Sporobolus pyramidalis	Stings and bites[19]	
Kantinka Herbaltics	*Spathodea campanulata*	Skin diseases, Sexualy Infections (STI)[20], stomach ache[21]	Gastritis, pelvic and chest pains, and skin infections.
	Mangifera indica	Chest pain[22]	
	Alstonia boonei	Antimicrobial[23]	

Microbiology Laboratory, Department of Microbiology, KNUST. The samples were analyzed in triplicate and the results reported as the mean standard deviation.[28]

pH determination

The pH of Mist Kantinka BA and Mist Kantinka Herbaltics was determined using a pH meter (Schott Instrument Lab 860; Schott Glass; Meinz, Germany) on a 20 mL sample at room temperature.

Preparation of sample and culture media

Mist Kantinka BA and Mist Kantinka Herbaltics were shaken vigorously to evenly disperse the microorganisms, if any. Stock samples were prepared by pipetting 5 mL aliquots each of Mist Kantinka BA and Mist Kantinka Herbaltics into 95 mL of sterile distilled water, followed by serial 10-fold dilutions in sterile test tubes. A one mL aliquot of the starting sample was aseptically transferred and mixed with 9 mL of sterile distilled water. All media used were prepared according to the manufacturer's instructions. For all viable bacteria and *E. coli*, appropriate solutions were transferred to duplicate sterile plates and 20 ml each of nutrient and MacConkey agar were added and mixed separately. For fungal enumeration, 1 ml each of Mist Kantinka BA and Mist Kantinka Herbaltics were streaked onto duplicate plates of prepared dried potato dextrose agar. Plates were incubated at 32°C for 48 hours for total plate counts, at 37°C for 24 hours for *E. coli* counts, and at 25°C for 5 days for bacterial counts. Plates were counted for total bacterial and fungal counts.

Antimicrobial testing

Ciprofloxacin tablets, fluconazole capsules, tetrazolium bromide solution, and the test organisms *C. albicans* and *N. gonorrhoeae* were obtained from the Department of Microbiology, KNUST, Ghana.

Minimum Inhibitory Concentration determination

Two-fold serial dilutions of the Kantinka BA and Kantinka Herbaltics were prepared in single-strength sterile Mueller Hinton broth (80-0.625% v/v). The ciprofloxacin and fluconazole used as standard drugs in the analysis were also prepared in two-fold dilutions (25-0.195 µg/mL). One hundred and eighty microlitres (180 uL) of the prepared concentrations were transferred into 96 well-bottom flat microtiter plates, 20 uL of *Neisseria gonorrhoeae* (NCTC12700) and *Candida albicans* (ATCC10031) cultures diluted and compared to 0.5 McFarland turbidity standard was added. All the plates were incubated at 37°C for 24 hours. After incubation, Minimum Inhibitory Concentrations (MICs) of the concentrations against test microbes were determined by the addition of 20 uL (0.125%) Tetrazolium bromide solution. After 30 minutes of addition of the dye, the wells were observed for inhibition or killing of microbial growth. All wells that stained purple color indicate microbial growth, and wells that remained yellow are indicative of inhibition.

Minimum Lethal Concentration determination

The Minimum Lethal Concentrations (MLCs) of the prepared concentrations were determined by subculturing 100 uL of all negative or yellow cultures contained in wells from the MIC determinations against test microbes into a fresh 100 uL sterile broth in 96 well plates. The plate was incubated at 37°C for another 24 hours and the results were observed for specific concentrations that kill 99.9% growth of the test microorganisms and recorded. All the assays were performed in triplicate.

Acute toxicity assessment of Kantinka BA and Kantinka Herbaltics

All experiments, and treatments were carried out on May 12, 2022, with the ethical approval code (AW/HM/KNUST/2023-052) obtained from the KNUST Animal Research and Ethics Committee. The acute oral toxicity of *Mist Kantinka BA* and *Mist Kantinka Herbaltics* were evaluated in Swiss albino rats according to the Organization for Economic Cooperation and Development (OECD) protocol. Nine nulliparous and non-pregnant animals (male n=5, female n=4) weighing 141-150 g, obtained from the Noguchi Memorial Institute for Medical Research were randomly selected and used for the study. The rats were fasted for 16 hours before the test commenced. The animals were maintained under ambient environmental conditions (22-25°C, 12 hours/12 hours light/dark cycle) and had free access to a standard pellet diet and water *ad libitum* before the start of the study. The study was conducted at the animal house of the Department of Pharmacology, KNUST. This study section adheres to the ARRIVE Guidelines for reporting animal research.[29]

In extract preparation, about 1000 mL of Mist Kantinka BA and Mist Kantinka Herbaltics was evaporated to dryness to obtain a semi-solid mass. The yield for Mist Kantinka Herbaltics and Mist Kantinka BA was 2.10% w/v and 2.53% w/v respectively. The obtained semi-solid mass was reconstituted to a 2000 mg/kg formulation and administered to test groups (n=3). The control group received 0.2 mL of distilled water (used to prepare doses of extracts). The animals were observed closely for 24 hours with much attention during the first four hours for altered autonomic effects such as lacrimation, salivation, piloerection, and central nervous system effects such as tremors, convulsion, and drowsiness. Changes in the body weight of rats were also monitored.[30] Per the protocol of the laboratory, the animals were kept for about two months and used for suitable assays as and when needed.

This was a cohort, retrospective clinical study to investigate outcomes of the co-administration of test samples to study participants by the review of the medical notes.

Study population, study design, and sample size calculation

This was a cohort, retrospective clinical study to investigate outcomes of the co-administration of test samples to study participants by the review of their medical notes. Two hundred patients visited the Tafo Government Hospital's Herbal Medicine Units and Adom Herbal Clinic between January 2014 and June 2022. The participants were newly diagnosed with Human Immunodeficiency Virus (HIV) / Acquired Immunodeficiency Syndrome (AIDS) and/or presented with the following symptoms: boils, cough, and skin infections. This was based on the inclusion and exclusion criteria. Outcomes measured were remission of boils, cough, and skin infections, which were presented.

Sample size was calculated using the formula:

$$\text{Sample Size (n)} = N \times \frac{(z^2 \times p \times (1-p))/e^2}{[N-1+(z^2 \times p \times (1-p))/e^2]}$$

where;
N= population size (200)
Z= critical value of the normal distribution at the required confidence level (1.96)
p= sample proportion (50%)

e= margin of error (95%)

Inclusion criteria

The inclusion criteria were: age above 18 years, newly diagnosed HIV/AIDS patients, patients who were not on any anti-viral or antibacterial therapy, patients who had reported for review for at least four clinic visits over the period of study, and the presence of cardinal signs and symptoms (boils, cough, skin infections, pruritus, and Pelvic Inflammatory Disease, PID).

Exclusion criteria

The exclusion criteria were age below 18, pregnant and lactating mothers, patients who had reported to the hospital once, and patients taking any allopathic or other alternative medication.

Experimental medication

Kantinka BA and *Kantinka Herbaltics* are prepared by Adom Herbal Clinic and Products, Tema, Ghana. The dosage for the two products is 45 mL thrice daily, thirty minutes before meals. It is taken for two weeks and repeated depending on the severity of symptoms and the presence of coexisting diseases. They are taken together.

Study completion criteria

The study completion criteria were that Kantinka BA and Kantinka Herbaltics would provide relief from boils, cough, skin infections, pruritus, and PID.

Ethical considerations

Consent and authorization to gather data for the study were approved by the Herbal Medicine Unit of the Tafo Government Hospital on January 5, 2022, with authorization reference number (TGH/09/39). The ethics committee waived the need for informed consent due to the retrospective nature of the human study.

Data collection

Records of the selected patients according to inclusion/exclusion criteria were examined to collect sociodemographic data, such as age and sex, and related data, such as symptoms (cough, pruritus, dyspepsia, and boils).

Effectiveness criteria

The effectiveness of Kantinka BA and Kantinka Herbaltics was evaluated based on the collected data. The criterion for effectiveness was the successful management of symptoms associated with HIV/AIDS.

Data analysis

Data on acute toxicity studies was analyzed using Graph Pad Prism (GraphPad Software; San Diego, USA) and presented as mean ± Standard Error of the Mean (SEM). Comparisons were made between the negative control group and treatment groups using one-way Analysis of Variance (ANOVA) followed by Dunnet's multiple comparison test. Data on clinical studies of Kantinka BA and Kantinka Herbaltics were statistically analyzed using Friedman's test to compare treatment effects across multiple test attempts from IBM Statistical Package for the Social Sciences (SPSS) (IBM Corp.; Armonk, USA).

Results

Phytochemical constituents of Kantinka Ba and Kantinka Herbaltics

The presence of tannins, reducing sugars, flavonoids, coumarins, and triterpenoids was detected in Kantinka BA, while alkaloids were also detected in Kantinka Herbaltics. However, phytosterols were not seen in either product (Table 2).

Microbial load content of Kaninka Ba and Kantinka Herbaltics

Evaluation of Kantinka BA and Kantinka Herbaltics for a load of microorganisms revealed pathogenic microbes such as *S. typhi, E. coli*, and *P. aeruginosa* absent from all product batches. Similarly, the total aerobic counts, yeast, and molds were within permissible levels. The batches did not differ from each other in microbial composition (Table 3).

pH

The pH of the different batches (n=5) was within a range of 5-7 for both products. There were differences observed between B1 and B2 and B2 and B3 for both products using Tukey's multiple comparisons test (Figure 1).

Acute toxicity

There were no gross physical and behavioural changes, such as rigidity, sleepiness, diarrhoea, abnormal secretion, or hair erection, for the first four hours following drug administration and subsequently 24 h. All the rats survived within the 2-week observation period.

Antimicrobial activities

The two products exhibited antimicrobial activities against the test organisms. The MIC and MLC determined for Kantinka BA

Table 2. Phytochemical constituents of Kaninka Ba and Kantinka Herbaltics.

Phytoconstituents	Kantinka BA	Kantinka Herbaltics
Tannins	+	+
Reducing sugars	+	+
Saponins	+	+
Alkaloids	-	+
Flavonoids	+	+
Coumarins	+	+
Triterpenoids	+	+
Phytosterols	-	-

+, detected; -, not detected

was 5% and <80 for *N. gonorrhea,* respectively, and 10% and <80, respectively, against *C. albicans*. For Kantinka Herbaltics, the MIC and MLC determined were 10% and <80% for *N. gonorrhea,* respectively, and 5% and <80, respectively, against *C. albicans*. Ciprofloxacin had both MIC and MLC at 0.390 µg/ml against *N. gonorrhoeae,* while fluconazole recorded MIC of 3.125 µg/ml and MLC of 12.50 µg/ml against *C. albicans* (Table 4). The antimicrobial activity of the products demonstrated an MIC ranging from 5 to 10 µg/mL for Kantinka BA and Kantinka Herbalitics, respectively, against *Neisseria gonorrhea* and *Candida albicans* and MLC of <80 for both products (Table 4).

Clinical study

In all, 117 (58.5%) of the participants were males and 83 (41.5%) were females (Figure 3). The age distribution of the participants shows that the ages of 29.6% of participants fall within the 18 to 25 years age group, 15.3% of participants fall within the 26 to 30 years age group, and 24.1% are within the age group of 31 to 40 years. Some 13.3% were in the age group of 41 to 50 years. Also, 17.7% of participants were above 51 years (Figure 4).

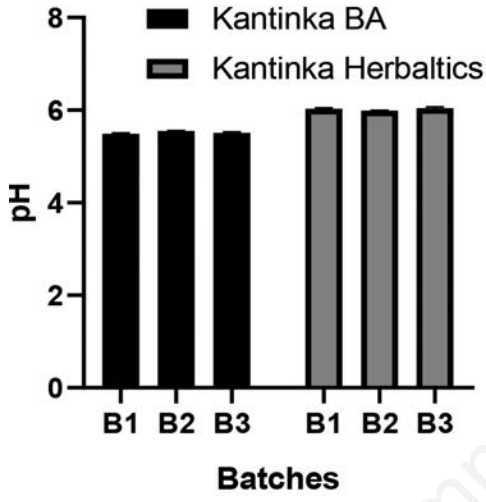

Figure 1. The pH of different batches of Kantinka BA and Kantinka Herbaltics.

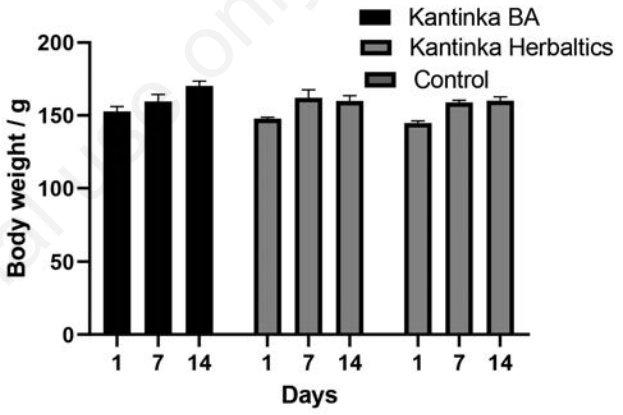

Figure 2. Body weight of experimental animals in acute toxicity assessment (n=3). Results were statistically significant at p<0.05.

Table 3. Microbial load of three different batches of Kantinka BA and Kantinka Herbaltics.

Microbes	Kantinka BA Microbial load (cfu/mL)			Kantinka Herbaltics Microbial load (cfu/mL)			*BP 2018
	B1	B2	B3	B1	B2	B3	
Total aerobic counts	$1.2x10^3$	$1.1x10^3$	$0.9x10^3$	$1.1x10^3$	$1.1x10^3$	$0.9x10^3$	$\leq 1.0x10^4$
Total yeast and moulds count	$1x10^2$	$0.9x10^2$	$1x10^2$	$0.9x10^2$	$0.9x10^2$	$1x10^2$	$\leq 1.0x10^2$
S. aureus	ND	ND	ND	ND	ND	ND	Absent in 1 mL
P. aeruginosa	ND	ND	ND	ND	ND	ND	Absent in 1 mL
E. coli	ND	ND	ND	ND	ND	ND	Absent in 1 mL
S. typhi	ND	ND	ND	ND	ND	ND	Absent in 1 mL

ND, Not Detected; B1, Batch 1; B2, Batch 2; B3, Batch 3; BP, British Pharmacopoeia standard 2018.

Table 4. Minimum Inhibitory Concentration (MIC) and Minimum Lethal Concentration (MLC) values of Kantinka BA and standard drugs concentrations recorded against test organisms.

Products/Standard drugs	Kantinka BA (%v/v)		Kantinka Herbaltics (%v/v)		Ciprofloxacin (µg/ml)		Fluconazole (µg/ml)	
Test organism	MIC	MLC	MIC	MLC	MIC	MLC	MIC	MLC
N. gonorrhoeae	5	<80	10	<80	0.390	0.390	NA	NA
C. albicans	10	<80	5	<80	NA	NA	3.125	12.50

MIC, Minimum Inhibitory Concentration; MLC, Minimum Lethal Concentration; NA, Not Applicable.

Clinical characteristics and effectiveness of samples

The symptoms that occurred most was cough, followed by pruritus, dyspepsia, and boils. Results of the analyses reveal statistically significant differences in severity of cough [$\chi^2(2)=58.876$, $p<0.001$], dyspepsia [$\chi^2(6)=225.05$, $p<0.001$], pruritus [$\chi^2(8)=259.91$, $p<0.001$] and boils [$\chi^2(4)=84.055$, $p<0.01$].

Discussion

The increasing use of medicinal plant products worldwide for treating various diseases calls into question the number of clinically unverified herbal products. Herbal medicines have historically been used to promote optimal health and well-being. They contain numerous phytocomponents that possess pharmacological activities.[32] Therefore, there is a need to exploit the potential clinical benefits of herbal products as an alternative to conventional medicine. This has many benefits for the many people who rely on herbal products for their primary healthcare needs, as it improves consumers' quality of life.

Kantinka BA *and* Kantinka Herbaltics were used in clinical practice in Ghana before integrating herbal medicine services into the healthcare delivery system for managing infectious diseases. However, there is no clinical data to validate their effectiveness and justify their continual utilization. Thus, it is desirable to undertake an observational experimental and clinical study of the two products using standard scientific methods to evaluate the effectiveness of their benefits in humans.

The therapeutic effects observed in plants are mainly attributed to their secondary metabolites (Table 1). Thus, the impact of Kantinka BA and Kantinka Herbaltics could result from the phytochemicals detected by the phytochemical assay.[33] Studies have been coupled with reports of the antimicrobial activities of tannins,[34,35] saponins,[36,37] alkaloids,[38,39] flavonoids[40,41] coumarins,[42,43] and triterpenoids.[44,45] Thus, the phytochemicals detected in the products could be acting alone, additively, or synergistically to produce the observed therapeutic effects (Table 1).

The formulation of aqueous preparations always presents the challenge of microbial contamination. This is mainly due to moisture providing an atmosphere for microbial growth.[46] In using crude drugs, a pure sample is seldom obtained for which limits are set to regulate the microbial contamination of samples in the quest to promote quality.[24] In the study, all microbes tested were within the WHO permissible limits (Table 3). This infers the safety of the products regarding microbial contamination.

It has been observed that the quality of herbal medicines can be assessed with the pH of their solutions. The pH of the decoctions of *both Kantinka BA* and *Kantinka Herbaltics* ranged 5-7 for all the batches tested (Figure 1). It is envisaged that decoctions obtained from adulterated materials and poorly kept samples may deviate mainly from the stated pH value. The low pH of substances in solution is known to inhibit the growth of pathogenic microorganisms and, consequently, help preserve medicinal products.[47] Although significant differences were observed in some samples, they all fall within standards and can be accepted.

Kantinka BA and Kantinka Herbaltics was found to be safe. No abnormality was observed. In the monitoring of the body weight changes (Figure 2), no significant changes were observed between the test groups and control groups ($p<0.05$, Dunnett's multiple comparisons test). Intra-group comparisons revealed significant body weight changes in the test animals that received them. Kantinka BA and Kantinka Herbaltics had no adverse effect following oral administration of a dose of 2000 mg/kg per body weight with no signs of acute toxicity. The LD_{50} was, therefore, estimated to be more than 2000 mg/kg body weight. All the rats survived, and physical observation did not reveal any signs of toxic

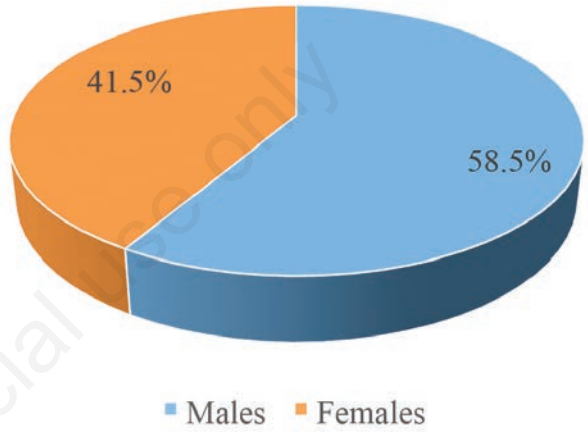

Figure 3. Gender distribution of participants..

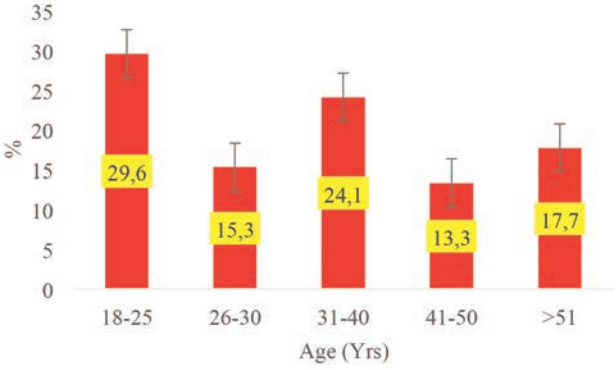

Figure 4. Age distribution of participants.

Table 5. Results of Friedman's test used in the clinical effectiveness of samples on infections.Products/Standard drugs Kantinka BA (%v/v)

Symptom	N	Test Statistic	df	p
Cough	53	58.876	2	0.000
Dyspepsia	49	225.05	6	0.000
Pruritus	52	259.91	8	0.000
Boils	31	84.055	4	0.001

effects such as changes in skin, eyes, and mucus, behavior patterns, trembling, diarrhea, falling of the fur, sleep, or coma. There was no significant body weight loss among the tested groups when compared to the control group (Figure 2). Also, no death was recorded for the 2-week observation period. This implies that both products may be safe using the dose listed on the labels.

The MIC of *Piper umbellatum*, an ingredient of Kantinka BA, when tested against Gram-negative bacteria, ranged from 12.5-25 µg/mL. The mode of action appeared to be associated with changes in the permeability of the bacterial membranes, as this resulted in increased penetration of hydrophobic antibiotics, efflux of K+, and nucleotide leakage.[48] According to a study on *Vernonia conferta*, another ingredient, hydroethanolic extracts, showed an antibacterial effect on the microbial strains responsible for diarrhea, with MIC values between 2 and 32 mg/mL.[49] The last ingredient, *Sporobolus pyramidalis*, also had antibacterial activity with MIC >2.5 mg/mL for all extracts tested.[50] The MIC of the methanol extract of *S. campanulata,* an ingredient of Kantinka Herbaltics, was: *C. albicans* (45-50 mg/mL), *B. subtilis*, and *E. coli* (50-55 mg/mL), *P. aeruginosa* (60-65 mg/mL), *S. aureus* (145-150 mg/mL). The ethanolic extract of *Mangifera indica* is active with minimum inhibitory concentration ranging from 5481.0 to 43750.0 µg/ml^{-1}.[51] Also, the antimicrobial activity of the extracts of *Alstonia boonei* revealed that the ethanolic extract produced a maximum zone of inhibition (23.73 mm) against *E. coli*. All extracts had no inhibitory effect on *Salmonella typhi* and *Pseudomonas aeruginosa* at the lowest concentration tested (3.2 mg/mL). The MIC was determined at different concentrations, and the lowest MIC (5.8 mg/mL) was produced by the crude ethanol extract on *E. col*i, while the ethanol extract on *E. coli*[52] also had the lowest minimum bactericidal concentration (20 mg/mL). This shows the effectiveness of the products as they showed higher antibacterial activity than the individual plants used alone. Consequently, the products can achieve higher therapeutic results than the individual extracts.

HIV/AIDS is mainly characterized by its immunodeficiency feature, and as such, paves the way for the thriving of various microbes and their associated infections. Thus, many rural dwellers, especially in developing countries such as Ghana, prefer using herbal products, which can treat diseases and their associated infections because of their vast array of constituents.[53] Kantinka BA and Kantinka Herbaltics, since the integration of herbal medicine services into the health delivery system, are administered together for the management of HIV/AIDS and its associated infections. In this study, the focus was on the common infections that present with HIV/AIDS, including cough, dyspepsia, pruritus, and boils. The results showed significant improvement for all the infections investigated among the patients. Subsequently, alleviating the symptoms of the presented infections would improve the patients' quality of life. Also, from the antibacterial activity observed against *N. gonorrhoeae* and *C. albicans* (Table 4), the products could combat gonorrhea and other Sexually Transmitted Infections (STIs) if the patients were infected. The outcome of this study supports a similar study that established the effectiveness of Kantinka BA and Kantinka Herbaltics used as a combination therapy in clinically diagnosed cases of HIV/AIDS at the Adom Herbal Clinic.[54]

Evidently, there was statistical significance for treating cough, dyspepsia, pruritus, and boils (0.01). Post-hoc analyses using Wilcoxon signed-rank test with the Bonferroni correction for pairwise comparison for all symptoms scenarios showed significant difference in severity between first and last visits for cough [Z=1.198, p<0.001], dyspepsia [Z=4.612, p<0.001], pruritus [Z=5.317, p<0.001] and boils [Z=3.097, p<0.001] (Table 5).

In summary, this study has established the antimicrobial activity, toxicity, and retrospective clinical effectiveness of Kantinka Ba and Kantinka Herbaltics. Kantinka Ba and Kantinka Herbaltics may contribute to improved quality of life and be useful in managing some signs and symptoms associated with infectious diseases. The study's diverse findings from patients of different age groups present its major strength. However, considering the breadth of the research topic, the study's purposive limited sample size and use of only herbal products somehow limit the transferability of the outcomes. Nevertheless, this study has improved the qualitative empirical evidence in respect of the use of herbal medicine in patients with infectious diseases in Ghana. Also, it has identified herbal products for infectious diseases. The effects of the test samples may be scientifically accepted to establish their effects and hence inform the health workforce and policymakers of their potential use in the health systems delivery in Ghana. Since qualitative outcomes may inform choice of interventions, this study calls for health professionals to work hand-in-hand with herbal medicine practitioners in improving healthcare, thereby preventing any potential complications associated to herbal medicine utilization. Such efforts may contribute to collaboration and provision of improved health services to patients.

Conclusions

The use of Kantinka BA and Kantinka Herbaltics in the management of infectious diseases and its associated infections and symptoms is validated based on the findings of the present study. The products are safe for consumption with an LD_{50} > greater than 2000 mg/kg. It is thus, concluded that *Kantinka BA* and *Kantinka Herbaltics* may be effective in the management of some infectious diseases and it associated symptoms such as cough, boils, dyspepsia and pruritus.

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