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Research Article

Effects of Ginger and Piroxicam Administration on the Electrolyte, Urea and Creatinine Levels of Wistar Albino Rats with Renal Pathology

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Abstract

The aim of the study was to assess the effects of ginger and piroxicam administration on the electrolyte, urea and creatinine levels of test and control wistar albino rats with renal pathology. Fifty albino rats were used for this study. They were divided into five (5) equal groups (labelled A to E) of ten (10) rats each. Group A served as the control. Group B were administered 2.7mg/kg of piroxicam, Group C were administered 400mg/kg of ginger, Group D were administered 2.7mg/kg of piroxicam and 100mg/kg ginger, Group E were administered 2.7mg/kg of piroxicam and 400mg/kg of ginger. The substance administration was given daily for 21 days (3 weeks) and the weights of both the test animal and control were monitored. After the administration, the rats were put under light chloroform anaesthesia and the blood samples were collected for Electrolytes, urea and creatinine processing. ANOVA was used to analyse the results of the weight and differences were considered significant at $P < 0.05$ level of confidence. All data are expressed as Mean±Standard error of mean (SEM). The result was presented in tables and comparison made statistically. The result shows the sodium ion, potassium ion, chloride ion, bicarbonate ion, urea and creatinine level of control and test subjects in which the Mean±SEM of sodium ion, potassium ion, chloride ion, bicarbonate ion, urea and creatinine level were 137.5±0.4282, 3.717±0.03073, 103.7±0.6667, 22.83±0.5426, 22.50±1.708 and 0.7167±0.04773 respectively for control subjects. The test groups for sodium ion, chloride ion and bicarbonate ion were statistically significant ($p<0.05$) with the control while the test group for potassium was highly significant ($p<0.001$) with its control. However, there was no statistical significance in urea and creatinine test groups when compared with the control. This study showed that oral administration of ginger and piroxicam in combination and individually, is associated with renal dysfunction, evident by serum electrolyte imbalance, leading to hyponatremia and hypercreatinemia. However, this might be beneficial in conditions associated with hypernatremia.

Keywords: Kidney, Renal failure, Ginger, Electrolyte, Urea, Creatinine, Piroxicam

Introduction

Kidney is very important organ particularly for filtering blood to discard unnecessary substances. The kidney showed many essential functions in the body such as remove waste products of metabolisms, maintain fluid and electrolyte balances and also the homeostasis system [1]. Impaired kidney function often results in chronic kidney disease (CKD) [2]. Chronic renal failure is a serious

problem in the world, in both developed and developing countries, which currently increased substantially. From a survey conducted by PERNEFRI (Association Nephrology Indonesia) in 2009, the prevalence of chronic renal failure in Indonesia approximately 12.5% which means that there are 18 million adults in Indonesia suffered from chronic renal failure [3].

Piroxicam is a nonsteroidal ant-inflammatory drug used to reduce pain, swelling, and joint stiffness from arthritis. Studies show that piroxicam (20 mg/day) compared to other Nonsteroidal anti-inflammatory drugs (NSAIDs) is more potent and less frequently employed daily, because of its long half-life, notably piroxicam in RA is equal to ibuprofen (400 mg 3-4 times a day), but better than indomethacin (25 mg administered 3 times daily). Piroxicam is slightly superior to naproxen (500 mg B.I.D) [4]. There is a high degree of "cross-sensitivity" between aspirin and other NSAIDs in patients who have symptoms of rhinitis or asthma, and the Genesis is pharmacologic rather than immunologic, compared to urticaria (on exposure to aspirin) in which mechanism is probably immunologic (salicylate metabolite), that does not correlate with other NSAIDs [5,6].

Ginger, the rhizome of the plant Zingiber officinale Roscoe, is widely used as a spice and herbal medicine for the treatment of catarrh, rheumatism, nervous diseases, gingivitis, toothache, asthma, stroke, constipation, and diabetes [7].

NSAIDs have wide therapeutic indices, however, widespread and chronic use of the drugs have been reported to increase the prevalence of their adverse effects [8]. Two most common adverse effects associated with NSAIDs are gastrointestinal (GI) toxicity- especially dyspepsia and gastric ulceration [9] and alteration in renal function [4,10]. NSAID-induced renal toxicity is dependent on the dose and duration of exposure. Short term (hours) administration of NSAIDs to susceptible individuals may cause acute renal failure (ARF), due to decrease in renal plasma flow (renal ischaemia) and glomerular filtration rate (GFR). The relative risk of renal toxicity among NSAIDs is not well known. Furthermore, NSAIDs are excreted by the kidneys with the implication that existing renal pathology in patients will increase their toxicities. It is therefore evident that knowledge on the relative renal effects of these agents is essential, more so, in view of their wide range of indications and consequent frequent usage. This will enhance their rational selection for patients and consequently reduce their toxicities. The aim of the study is to assess the effects of ginger and piroxicam administration on the electrolyte, urea and creatinine levels of test and control wistar albino rats.

Materials and Methods

This study was carried out in the experimental site of Department of Histopathology, Ambrose Alli University, Ekpoma, Edo State.

Research Design

Fifty albino rats were used for this study. They were divided into five (5) equal groups (labelled A to E) of ten (10) rats each. Group A served as the control. Group B were administered 2.7mg/kg of piroxicam, Group C were administered 400mg/kg of ginger, Group D were administered 2.7mg/kg of piroxicam and 100mg/kg ginger, Group E were administered 2.7mg/kg of piroxicam and 400mg/kg of ginger. The substance administration was given daily for 21 days (3 weeks) and the weights of both the test animal and control were monitored. After the administration, the rats were put under light chloroform anaesthesia and the blood samples were collected for Electrolytes, urea and creatinine processing. ANOVA was used to analyze the results of the weight and differences were considered significant at $P < 0.05$ level of confidence. All data are expressed as Mean±Standard error of mean (SEM). The results were presented in tables and comparisons made statistically.

Ethical Approval

The protocol for this study was approved by the Ethics and Research Committee of the Ambrose Alli University, Ekpoma, Edo State.

Experimental Animals/Housing Condition

Fifty (50) Adult albino rats of comparable sizes and weights ranging from 90g to 130g were procured from the Animal Farm, histopathology, Ekpoma, Edo State and transferred to the experimental Laboratory histopathology, where they were allowed two (2) weeks of acclimatization. They were kept in wire mesh cages with tripod that separates the animal from its faeces to prevent contamination. During this period of acclimatization, the rats will be fed with Growers' mash and water ad libitum. The animals were maintained and utilized in accordance with the standard guide for the care and use of Laboratory animals.

Animal Grouping

The experimental animals were separated into five groups (A-E). Each group contains ten rats each (n = 10) using five (5) big cages to house them. Group A served as the control, while groups B - E served as the test groups.

Study Duration

The preliminary studies, animal acclimatization, drug and substance procurement (dosage preparation and reconstitution), actual animal experiment and evaluation of results, lasted for a period of five months.

Substance Administration

Group A (Control) received only normal feed (growers' mash) and water daily.

Group B were administered 2.7mg/kg of piroxicam.

Group C were administered 400mg/kg of ginger.

Group D were administered 2.7mg/kg of piroxicam and 100mg/kg ginger.

Group E were administered 2.7mg/kg of piroxicam and 400mg/kg of ginger.

Sample collection and Analysis

Weight was measured before and after acclimatization and similar weight measurements were done at the end of each week and the average weight recorded accordingly. The electrolyte, ureas and creatinine levels of piroxicam and ginger induced rats were determined calorimetrically using standard laboratory procedure.

Renal Function Tests

Method for chloride, sodium, potassium and bicarbonate ion Estimation (ISE): Chloride, sodium, potassium and bicarbonate was estimated using Ion selective electrode.

Procedure: When ISE gets contact with the measured solution, the measured ion in the sample goes to ISE membrane due to the diffusion effects of the concentration difference, which created a potential between measure electrode and reference electrode.

Calculation: Ion selective electrode (ISE) is a kind of electrochemical sensor (also called electrode), the activity changes of specific ion could be converted into the electrical potential changes of electrode, the relation accord with Nernst equation.

$$E = \left[\frac{E0 + 2.3026RT\ Log10a(x)}{ZF} \right]$$

E0: Electrode standard potential; R: Gas constant; T: Absolute temperature

F: Faraday constant; Z: Ion valence; a (x): Ion activity.

Creatinine Estimation

Creatinine was estimated by using Modified Jaffe's method.

Procedure: Bring the working reagent and the photometer to 37°C. Pipette into a cuvette 1.0ml of working reagent and 0.1ml of standard/sample. Mix and insert cuvette into the photometer. Start the stopwatch. Record the absorbance at 500nm after 30seconds (A2) and after 90 seconds (A2)

Calculation: The creatinine concentration in the sample is calculated using the following general formula

$$\frac{(A2\text{-}A1)\,\text{Sample}}{(A2\text{-}A1)\,\text{Standard}} \times \text{cocentration of standard} \times \text{Dilution Factor}$$

NORMAL RANGE: 0.7-.4mg/dl

Urea Estimation

Urea was estimated Calorimetrically bt Urease-Berthelot's Method.

Procedure: 10ul of sample, standard and distilled water was added to sample, standard and reagent blank test tube. 100ul of reagent I was added to all test tubes respectively. Mix and incubate at 37°C. Add 2.5ml of reagent II and reagent III to all test tubes respectively. Mix immediately and incubate at 37°C for 15mins.

Reading: Wavelength: 546nm; Blank: Reagent black; Colour: Stable for at least 8 hour.

$$\text{Calculation:} \frac{\text{Abs of Test}}{\text{Abs of standard}} \times \text{concentration of standard } (80)\,\text{mg/dl}$$

Statistical Analysis

Analysis of variance (ANOVA) at P≤0.05 level of significance shall be used to compare results in both the control and the test groups (all results shall be reported as mean±standard deviation); using a computer program named SPSS for windows release 20.0. confident interval Values P±0.05 shall be considered significant.

Results

Baseline Weight, Weight after Acclimatization and Before Sacrifice of Control and Test Subjects.

Table 1 shows the baseline weight, weight after acclimatization and before sacrifice of control and test subjects in which the Mean±SEM of baseline weight, weight after acclimatization, weight before sacrifice were 247.00±3.35, 219±9.36 and 219±6.40respectively for control subjects. None of the test groups were found statistically significant (p<0.05) when compared with their respective control.

Table 1: The mean difference in weights of the rats in various groups (A, B, C, D, E) using ANOVA.

Weight	Group A (Control)	Test group				F Value	P value
	(N=10)	Group B (N=10)	Group C (N=10)	Group D (N=10)	Group E (N=10)		
Baseline weight (gram)	247.00±3.35	244.00±1.63	244.00±1.63	241.00±1.80	241.00±1.80	1.37	0.2596
After acclimatization (gram)	249.00±9.36	236.70±4.41	226.70±8.03	240.00±4.47	241.00±2.33	2.3	0.0782
Before sacrifice (gram)	248.00±6.40	221.10±10.20	221.70±10.14	240.00±4.47	205.00±13.76	1.172	0.3399

*Means statistically significant (p<0.05)

Table 2: The mean and standard deviation of Na, K Cl, HCO3 Urea Creatinine level of various groups (A, B, C, D, E).

Electrolytes	Mean ± SEM of Control (Group A)	Mean ± SEM of Test group (Group B-E)	t	p-Value
Na+ (mmol/L)	137.5 ± 0.4282	144.4 ± 1.419	2.146	0.0391*
K+ (mmol/L)	3.717 ± 0.03073	3.153 ±0.05983	4.143	0.0002***
Cl- (mmol/L)	103.7 ± 0.6667	109.8 ± 1.097	2.456	0.0193*
HCO3- (mmol/L)	22.83 ± 0.5426	19.30 ± 0.4101	3.699	0.0008*
Urea (mg/dl)	22.50 ± 1.708	41.43 ± 4.396	1.899	0.0661
Creatinine (mg/dl)	0.7167 ± 0.04773	1.317 ± 0.1717	1.542	0.1323

*Means significant p<0.05: ***Means highly significant p<0.001

Table 2 shows the sodium ion, potassium ion, chloride ion, bicarbonate ion, urea and creatinine level of control and test subjects in which the Mean±SEM of sodium ion, potassium ion, chloride ion, bicarbonate ion, urea and creatinine level were 137.5±0.4282, 3.717±0.03073, 103.7±0.6667, 22.83±0.5426, 22.50±1.708 and 0.7167±0.04773 respectively for control subjects. The test groups for sodium ion, chloride ion and bicarbonate ion were statistically significant (p<0.05) with their respective control while the test group for potassium was highly significant (p<0.001) with its control. However, there was no statistical significance in Urea and creatinine test groups when compared with their respective control.

Table 3 shows the post Hoc test for control group and the test groups. Sodium ion concentration for the test groups except group C were each found to be highly statistically significant (p<0.001) when compared with control. Group C and D were also highly significant (p<0.001) when compared with group B. In addition, group D and E were highly significant (p<0.001) when compared with group C while group E was also statistically significant (p<0.05) when compared to group D.

Table 3: Comparison of the Weight and Parameters used.

Parameters	CONTROL Test Groups					f- value	p- value
	A	B	C	D	E		
Na^+ (mmol/L)	137.5±0.43	152.8±1.70***	135.2±0.65###β	144.7±1.38***###ααα	150±1.13***αααβ	50.95	0.0001***
K^+ (mmol/L)	3.717±0.03	2.75±0.02***	3.54±0.03###	3.129±0.07***###ααα	2.971±0.04***#ααα	76.34	0.0001***
Cl^- (mmol/L)	103.7±0.67	116.8±0.87***	102.7±0.82###	110.3±0.94***###ααα	113.4±0.87***ααα	50.73	0.0001***
HCO_3^-(mmol/L)	22.83±0.54	16.83±0.31***	21.7±0.56###	19.14±0.46***#αα	18.14±0.26***ααα	25	0.0001***
Urea (mg/dl)	22.5±1.71	80.17±2.60***	15.6±1.32###	37.29±1.90***###ααα	49.29±1.34***###αααβββ	207.3	0.0001***
Creatinine (mg/dl)	0.7167±0.05	2.95±0.12***	0.39±0.05**###	1.171±0.06***###ααα	1.386±0.04***###ααα	215.6	0.0001***

*** means statistically significant with control; p<0.001

** means statistically significant with control; p<0.01

###means statistically significant with group A; p<0.001

#means statistically significant with group A; p<0.05

ααα means statistically significant with group B; p<0.001

αα means statistically significant with group B; p<0.01

βββ means statistically significant with group C; p<0.001

β means statistically significant with group C; p<0.05

Potassium ion concentration for the test groups except group C were each found to be highly statistically significant (p<0.001) when compared with control. Group C and D were also highly significant (p<0.001) while group E has a significant P< 0.05 when compared with group B. In addition, group D and E were highly significant (p<0.001) when compared with group C.

Chloride ion concentration for the test groups except group C were each found to be highly statistically significant (p<0.001) when compared with control. Group C and D were also highly sig-

nificant (p<0.001) when compared with group B. In addition, group D and E were highly significant (p<0.001) when compared with group C.

Bicarbonate ion concentration for the test groups except group C were each found to be highly statistically significant (p<0.001) when compared with control. Group C and D were also significant (p<0.001 and p<0.05 respectively) when compared with group B. In addition, group D and E were significant (p<0.01 and p<0.001 respectively) when compared with group C.

Urea level for the test groups except group C were each found to be highly statistically significant (p<0.001) when compared with control. Group C, D and E were also highly significant (p<0.001) when compared with group B. In addition, group D and E were highly significant (p<0.001) when compared with group C while group E was also highly statistically significant (p<0.001) when compared to group D.

Creatinine level for the test groups were each found to be highly statistically significant (p<0.001 and p<0.01 for group C) when compared with control. Group C and D were also highly significant (p<0.001) when compared with group B. In addition, group D and E were highly significant (p<0.001) when compared with group C.

Discussion

Ginger kidney protective effect has been of limited value as previous studies was not randomized with common drug toxicity. Piroxicam on the other hand, has a potent inhibitor of prostaglandins, is effective and well-tolerated in the treatment of primary dysmenorrhea [11]. The aim of this study was to evaluate the effect of ginger (*zingiber officinale*) extracts on kidney administered with graded doses of piroxicam. The results of this study shows that there was no significant (p<0.05) difference in the body weight across all the groups. Therefore, the change in the body weight was not due to the administration of the substance but due the feed intake.

The result showed that the potassium ion concentration test for the groups, all groups except Group C showed a highly statistically significant (P<0.001) decrease when compared to their relative control groups. Also, Group C and Group D also showed a highly statistically significant (P< 0.001) decrease when compared with Group B. Group E showed a statistically significant (P < 0.05) decrease. Chloride ion concentration for the test groups, Group B, Group D and Group E showed a highly statistically significant (P< 0.001) increase when compared to the control groups. Group D were found to also be statistically significant (P < 0.001) when compared to Group B. However, Group C showed a statistically significant (P<0.001) decrease when compared to control group. This appears to be the first study to investigate and document changes in serum electrolytes as indices of renal function following Piroxicam and Ginger extracts in association. This is in tandem with findings of the previous studies [12].

Sodium is the most abundant extracellular ion, and it plays an important role in muscle contraction. Similarly, potassium, an abundant intracellular ion, plays a vital role in muscle contraction. The electrolyte derangement resulting from the reduced serum level of sodium seen in this study thus provides evidence that the use of aloe could present a risk for arrhythmia, abdominal pain and cramping, and muscle weakness. The observation that piroxicam and ginger induces electrolyte imbalance corroborates findings in the previous study that reported its laxative properties. It causes excess water loss accompanied by sodium loss, thus contracting the extracellular fluid with resultant electrolyte imbalance and consequent impairment of muscle contraction.

Ranganath and Gould [13] associated reduction in sodium and potassium ions with the increased bicarbonate level. This study seems to be the first to report the effect of aloe on plasma pH by evaluating serum bicarbonate concentration. The Bicarbonate ion concentration for the test groups revealed a highly statistically significant (P<0.001) decrease when compared with control. Group C and D were also significant (P<0.001 and P<0.05 respectively) increase when compared with Group B. Furthermore, Group D and E showed a statistically significant (P<0.01 and P<0.001 respectively) decrease when compared with Group C. Therefore, this shows that aloe-induced electrolyte imbalance evident by low plasma level of sodium, though significant, was not enough to cause metabolic alkalosis.

Creatinine clearance calculated from creatinine concentrations in urine and plasma samples, and the urine flow rate, as well as urea clearance, is used to determine the glomerular filtration rate of the kidneys. Although not commonly done anymore, they remain useful tests for renal function. Thus, plasma concentrations of creatinine and urea could be used as indicators of nephrotoxicity [14]. Low clearance of creatinine or/and urea indicates a diminished impaired ability of the kidneys to filter these waste products from the blood and excrete them in urine. As their clearance values decrease, their blood levels increase. Hence, an abnormally elevated blood creatinine is diagnostic of impaired renal function [14].

This study revealed that aloe induces a significant rise in serum creatinine. This is in consonance with the study of *Khairy, et al.,* [15] that reported the cytotoxic effect of Ginger and piroxicam. This study suggests that Ginger and Piroxicam in combination or individually, promotes nephrotoxicity, thus causing impaired renal function evident by an increase in serum creatinine concentration. This could also explain the electrolyte imbalance associated with the aloe use. The altered level of plasma sodium seen in aloe treatment might be as a result of sodium loss due to its cytotoxic effect. It is noteworthy that hyponatremia is a major challenge associated with the aloe use, however, if given with close monitoring of serum electrolytes might be beneficial in conditions associated with hypernatremia.

Urea concentration for the test groups showed that across in all

groups except Group C, each was found to have shown a highly statistically significant (P<0.001) increase when compared with control. Group C, D and E also showed a highly statistically significant (P<0.001) decrease when compared with Group B. Also, Group D and E showed a highly significant (P<0.001) increase when compared with Group C while Group E also revealed a highly statistically significant (P<0.001) increase when compared to Group D. The test for the concentration of creatinine in the test groups showed that all the groups have a highly statistically significant (P<0.01) increase when compared with control. Group C and D also showed a highly statistically significant (P<0.001 for Group C and P<0.001 for Group D) decrease when compared with group B. In addition, group D and E showed a highly significant (P<0.001) increase when compared with group C.

In this study, generally, the administration of the different extract resulted in significantly (P < 0.05) lower values in respective groups compared to as observed in control group i.e., group A. The value observed in group A is lower than as reported for control subjects in a similar toxicological study [16]. The pattern of change observed on administration of the respective doses of extracts simulate that reported for a study of the effect of ginger and piroxicam extract on blood urea nitrogen [17]. It has been opined that reduction of BUN in animals suggest a mechanism of reabsorption inhibition of urea in the nephron. This could be due to the fact that these extracts cause reduction of BUN in animals suggest a mechanism of reabsorption inhibition of urea in the nephron. The relation of urea to water reabsorption can cause cellular contraction and high concentration of substances like creatinine in plasma [17,18]. The significant decrease in BUN observed with administration of the different doses can be seen as having protective effect on renal tissue as elevated values have been considered to be toxic to renal tissue [16].

Conclusion

In conclusion, this study showed that oral administration of ginger and piroxicam in combination and individually, is associated with renal dysfunction, evident by serum electrolyte imbalance, leading to hyponatremia and hypercreatinemia. However, this might be beneficial in conditions associated with hypernatremia. Based on the biochemical observations acknowledged in this present study, it may be concluded that there is need for further study to determine accurately the effect of introduction of mild moderate and high dosage of *Zingiber officinale* (ginger) effects on the electrolytes level of individual on with varying doses of Piroxicam.

Conflict of Interest

The authors declare no conflicts of interest. The authors alone are responsible for the content and the writing of the paper.

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Authors' Contributions

The entire study procedure was conducted with the involvement of all writers.

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References

1. Kelly L (2004) Essentials of Human Physiology for Pharmacy. CRC Press, Florida, USA. pp. 105-156.
2. Dowling TC (2005) Renal Disorders, dalam Pharmacotherapy a Pathophsiologic Approach Edisi 7. The McGraw Hill Companies Inc, New York, USA, pp. 705-835.
3. PERNEFRI (2009) Annual Meeting 2009. Perhimpunan Nefrologi Indonesia.
4. Goodman ZD (2017) Phenotypes and pathology of drug-induced liver disease. Clin Liver Dis 21(1): 89-101.
5. Bessone F (2010) Non-steroidal anti-inflammatory drugs: What is the actual risk of liver damage? World J Gastroenterol 16(45): 5651-5661.
6. Lapeyre-Mestre M, Grolleau S, Montastruc JL (2013) Adverse drug reactions associated with the use of NSAIDs: A case/noncase analysis of spontaneous reports from the French pharmacovigilance database 2002-2006. Fundam Clin Pharmacol 27(2): 223-230.
7. Caballeria E, Masso RM, Arago JV Sanchis A (1990) Piroxicam hepatotoxicity. Am J Gastroenterol 85(7): 898-899.
8. Usui K, Oda Y, Kubota R, Negishi K, Uno K, et al. (2007) Clinical application of the leukocyte migration test and new diagnostic criteria for identifying causative agents in patients with drug-induced liver injury. Hepatogastroenterology 54(78): 1752-1757.
9. Reuben A, Koch DG, Lee WM (2010) Acute Liver Failure Study Group. Drug-induced acute liver failure: Results of a U.S. multicenter, prospective study. Hepatology 52(6): 2065-2076.
10. Rostom A, Goldkind L, Laine L (2005) Nonsteroidal anti-inflammatory drugs and hepatic toxicity: A systematic review of randomized controlled trials in arthritis patients. Clin Gastroenterol Hepatol 3(5): 489-498.
11. Gabr SA, Alghadir AH, Ghoniem GA (2019) Biological activities of ginger against cadmium-induced renal toxicity. Saudi Journal of Biological Sciences 26(2): 382-389.
12. Kirdpon S, Kirdpon W, Airarat W, Trevanich A, Nanakorn S (2006) Effect of aloe (Aloe vera Linn.) on healthy adult volunteers: Changes in urinary composition. J Med Assoc Thai 89(Suppl 2): S9-S14.
13. Ranganath LR, Gould SR (1999) Postural hypotension and electrolyte disturbance in a 6year old man. Postgrad Med J 75(881): 185-187.
14. Henry JB (2001) Clinical Diagnosis and Management by Laboratory Methods. 20th Edition, WB Saunders Company, Philadelphia, USA pp. 17-19.
15. Khairy A, Ghareeb DA, Celik I, Hammoda HM, Zaatout HH, et al. (2023) Forecasting of potential anti-inflammatory targets of some

immunomodulatory plants and their constituents using in vitro, molecular docking and network pharmacology-based analysis. Sci Rep 13(1): 9539.

16. Asomugha RN, Okafor PN, Ijeh II, Orisakwe OE, Asomugha AL, et al. (2013) Toxicological evaluation of aqueous leaf extract of Chromolaena Odorata in male Wistar albino rats. J Appl Pharm Sci 3(12): 89-92.

17. Mehrdad M, Messripour M, Ghobadipour M (2007) The effect of ginger extract on blood urea nitrogen and creatinine in mice. Pak J Biol Sci 10(17): 2968-2971.

18. http://www.google.com/wikipedia/geographical/regional/location.