Journal of Pharmacology and Toxicology

ISSN 1816-496X

Academic Journals Inc.

www.academicjournals.com

OPEN ACCESS Journal of Pharmacology and Toxicology

ISSN 1816-496X
DOI: 10.3923/jpt.2023.83.88

Research Article
Toxicity Studies of *Physalis angulata* Leaves Extract on Biochemical and Haematological Parameters in Albino Rats

[1]Rita M. Sunday and [2]Olapade R. Ilesanmi

[1]Department of Medical Biotechnology, National Biotechnology Development Agency, Abuja, Nigeria
[2]Department of Pharmacology, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, Osun, Nigeria

Abstract

Background and Objective: The plant, *Physalis angulata* is used in ethnomedicine for the treatment of various diseases. The acute and sub-chronic toxicity of *Physalis angulata* L. Leaves ethanolic extract was investigated in this study using an *in vivo* model (albino rats). **Materials and Methods:** The plant extract was orally administered to albino rats once in the acute toxicity study and daily for 21 days in the sub-chronic toxicity study. Distilled water (5 mL kg^{-1} b.wt.) was administered to animals in the control group. 50, 100 and 200 mg extract/kg body weight was administered to the animals in the treatment groups. The median lethal dose of the plant extract was determined in the acute toxicity study. In sub-chronic toxicity studies, the effect of *Physalis angulata* leaves extract on body weight, food intake, water intake, biochemical (alanine transaminase, aspartate transaminase, creatinine and cholesterol) and haematological (packed cell volume, red blood cells and white blood cells) parameters were determined. **Results:** *Physalis angulata* leaves ethanolic extract caused no mortality of animals all through the study. In the acute toxicity study, the median lethal dose of *Physalis angulata* leaves ethanolic extract was greater than 5000 mg kg^{-1}. *Physalis angulata* leaves ethanolic extract caused a reduction in cholesterol concentration and an increase in red blood cells in the sub-chronic toxicity studies when compared with the control. **Conclusion:** The results suggested that *Physalis angulata* leaves ethanolic extract at the dose administered caused no toxic effect when orally administered acutely and daily for 21 days in albino rats.

Key words: *Physalis angulata*, leaves, toxicity, haematology, alanine transaminase, packed cell volume, creatinine

Citation: Sunday, R.M. and O.R. Ilesanmi, 2023. Toxicity studies of *Physalis angulata* leaves extract on biochemical and haematological parameters in albino rats. J. Pharmacol. Toxicol., 18: 83-88.

Corresponding Author: Rita M. Sunday, Department of Medical Biotechnology, National Biotechnology Development Agency, Abuja, Nigeria

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Physalis angulata L., is a medicinal plant that belongs to the family Solanaceae and it is found in sub-tropical and tropical regions. *Physalis angulata* is commonly known as wild gooseberry and cut leaf groundcherry in English. In Nigeria, it is known as Saadi Birii in the Hausa language and koropo in the Yoruba language. The plant is used in traditional medicine for the relief of pain (analgesic) and the treatment of numerous diseases including cough, fever, malaria, inflammations and asthma[1]. Previous studies reported that *Physalis angulata* have antimicrobial[1,2], anticancer[3], immunomodulatory[4], anti-inflammatory[5], neouroprotective[6], anti-oxidant[7] and anti-malarial activity[8]. *Physalis angulata* is used as a medicinal plant in different parts of the world for the treatment of numerous diseases[9]. In Kenya, the whole plant is used for the treatment of stomach ache[10]. The whole plant is also used in Nigeria for the treatment of gonorrhoea, diabetes, rashes and malaria[11]. *Physalis angulata* root is used in Bolivia for the treatment of fever[12] and in Indonesia, it is used for the treatment of muscle aches and hepatitis[13]. The plant root is also used in Brazil for the treatment of hepatitis, anaemia, ear pain and diabetes[14]. The leaves of *Physalis angulata* are used in India for the treatment of wounds[15] and in Equatorial Guinea, they are used as anti-dermatitis[16].

Plants with medicinal properties have been used from time immemorial for the treatment and management of diseases. About 80% of people worldwide use medicinal plants for their health care[17]. These have led to concerns about the toxicity and safety levels of medicinal plants used in traditional medicine for the treatment of diseases[18]. Symptoms of toxicity include diarrhoea, stomach ache, nausea, vomiting, liver damage and in some cases mortality[19].

This study was carried out to determine the acute and sub-chronic toxicity of *Physalis angulata* leaves ethanolic extract due to its use in traditional medicine for the treatment of diseases.

MATERIALS AND METHODS

Study area: The study was carried out at Obafemi Awolowo University, Ile-Ife, Nigeria and National Biotechnology Development Agency, Abuja, Nigeria and it was completed in the year 2022.

Plant material: *Physalis angulata* leaves were gotten from Ogbomoso, Oyo State, Nigeria. The plant was authenticated at Ife herbarium, Department of Botany, Obafemi Awolowo University (O.A.U), Ile-Ife, Osun State, Nigeria.

Extraction procedure: *Physalis angulata* leaves were washed under clean running tap water and then oven-dried (40°C). The dried plant sample was ground into powder, soaked in ethanol (70%) for 72 hrs and filtered using Whatman no.1 filter paper. The filtrate was concentrated into a solid paste using a rotary evaporator and then dried using a freeze drier. The dried plant extract was used for the study[20].

Animals: The approved guidelines (experiment using animals) of the Department of Pharmacology, Faculty of Pharmacy O.A.U, Ile-Ife, Osun State, Nigeria was used for the experimental study.

Thirty-six albino rats of both sexes weighing 160-165 g were gotten from Animal House, Department of Pharmacology, Faculty of Pharmacy, O.A.U, Ile-Ife, Osun State, Nigeria.

Acute toxicity study: The acute toxicity of *Physalis angulata* leaves ethanolic extract was determined in albino rats after administration of the extract via the oral route (p.o.)[21]. The study on acute toxicity was in phases. Phase 1: Three animals in each group (groups 1, 2 and 3) were administered 10, 100 and 1000 mg kg^{-1}. They were then observed at 10, 30, 60 and 120 min and at 4, 6 and 24 hrs for signs of toxicity which include distress in respiration and mortality. The animals were further observed daily for 14 days. In phase 2, higher doses were administered to the animals because there was no mortality of albino rats in the phase 1 study. A fresh set of three animals was used in phase 2 and was divided into three groups with a rat each. Animals in each group were administered the plant extract at 1600, 2900 and 5,000 mg kg^{-1} and were observed as in phase 1. The Median Lethal Dose (LD_{50}) was determined at the end of the acute toxicity study.

Sub-chronic toxicity study: Twenty-four albino rats of both sexes were divided into four groups of six rats each. Albino rats in groups 1, 2 and 3 were orally administered 50, 100 and 200 mg extract/kg body weight, respectively daily for 21 days[20]. Animals in group 4 were orally administered 10 mL distilled water/kg body weight daily for 21 days[20]. The animals had free access to water and food throughout the experiment and they were observed daily for symptoms of toxicity. The animals were deprived of food and water for 24 hrs before they were sacrificed on day 22. Each animal was sacrificed (under diethyl ether anaesthesia) and blood was collected by cardiac puncture for biochemical (serum) and haematological (plasma) analysis. Biochemical parameters analysed include aspartate aminotransferase, alanine aminotransferase[22], creatinine[23] and total cholesterol[24] concentration determination. Haematological parameters screened include

packed cell volume, red blood cell count and white blood cell count. The change in body weight of the animals, volume (mL) of water and weight (g) of food consumed by the animals in each group on days 7, 14 and 21 were determined.

Statistical analysis: The results were analyzed using One-way Analysis of Variance (ANOVA) followed by Tukey's pairwise comparisons tests at 95% ($p<0.05$) level of significance using Paleontological Statistics (version 3.23). All results were expressed as Mean±Standard error of the mean (SEM).

RESULTS

Acute toxicity and median lethal dose of *Physalis angulata* leaves: *Physalis angulata* leaves ethanolic extract caused no mortality in albino rats and there were no signs of toxicity such as diarrhoea, nausea and vomiting. The Median Lethal Dose (LD_{50}) of *Physalis angulata* leaves ethanolic extract was $\geq$5000 mg kg^{-1} (via the oral route of administration).

Effect of *Physalis angulata* leaves ethanolic extract on body weight (g): *Physalis angulata* leaves ethanolic extract caused no significant ($p<0.05$) change in the body weight of albino rats when compared with the control (Fig. 1).

Effect of *Physalis angulata* leaves ethanolic extract on food (g) intake: *Physalis angulata* leaves ethanolic extract exerted no significant ($p<0.05$) change in food intake by albino rats when compared with the control (Fig. 2).

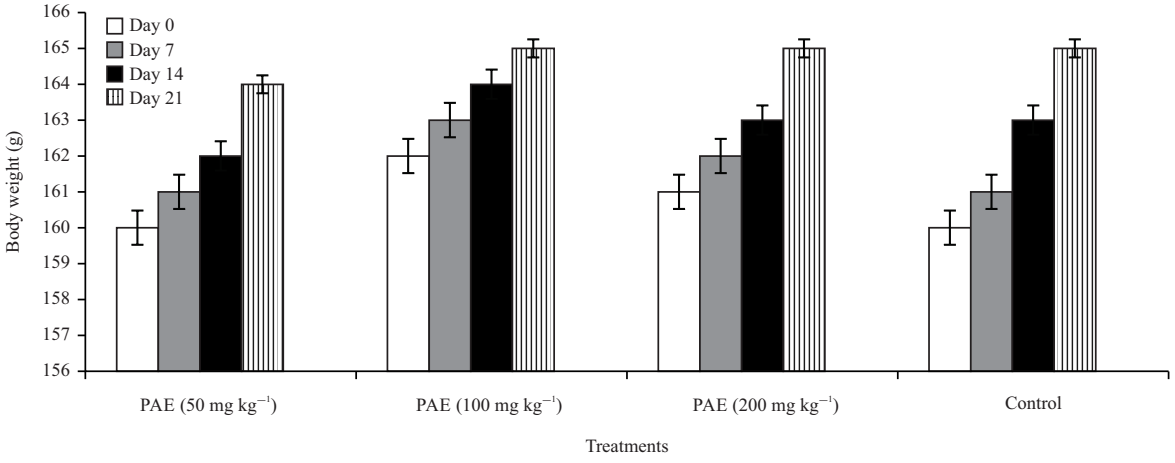

Fig. 1: Effect of *Physalis angulata* leaves ethanolic extract on body weight (g) of albino rats
Data are expressed as Mean±SEM, n = 6 and PAE: *Physalis angulata* leaves ethanolic extract

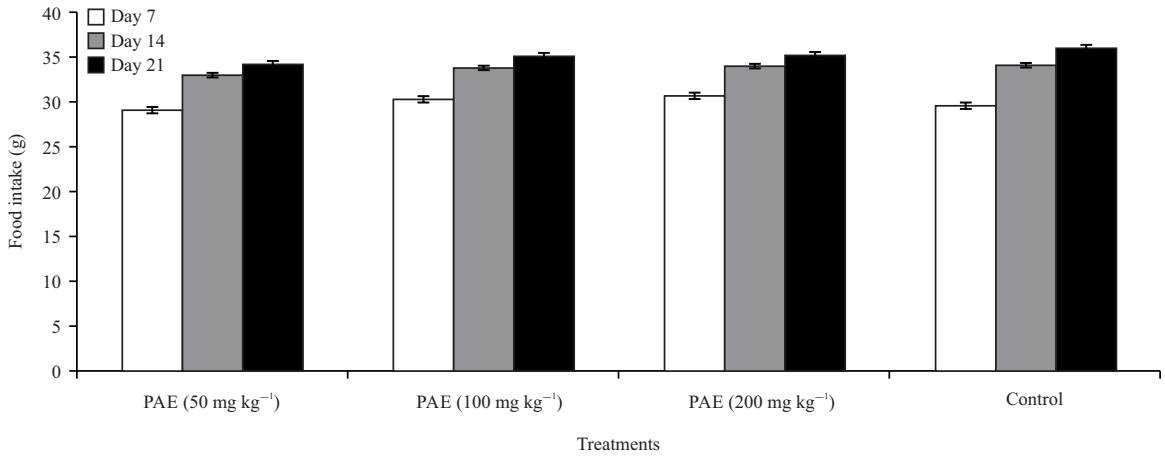

Fig. 2: Effect of *Physalis angulata* leaves ethanolic extract on food (g) intake by albino rats
PAE: *Physalis angulata* leaves ethanolic extract, data are expressed as Mean±SEM and n = 6

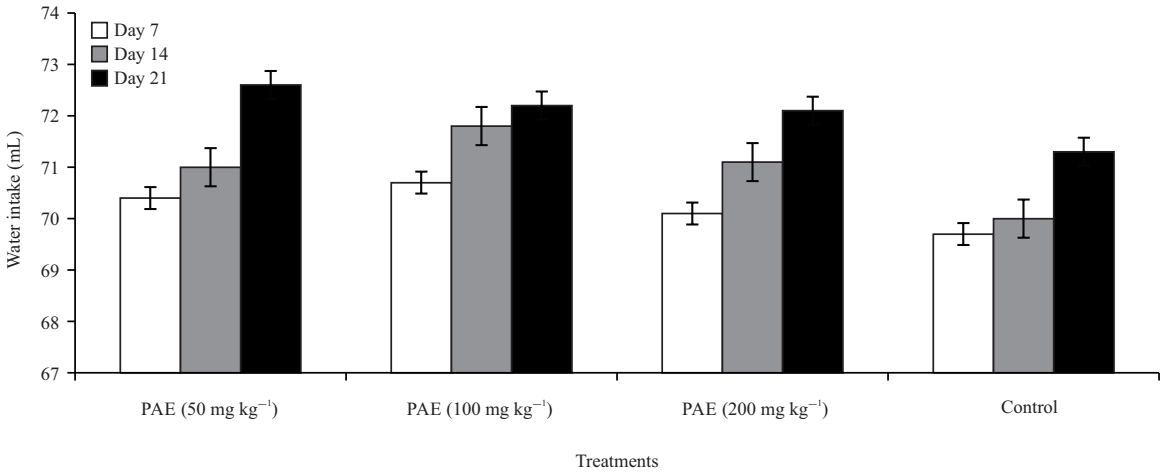

Fig. 3: Effect of *Physalis angulata* leaves ethanolic extract on change in water (mL) intake by albino rats
PAE: *Physalis angulata* leaves ethanolic extract, data are expressed as Mean±SEM and n = 6

Table 1: Effect of *Physalis angulata* leaves ethanolic extract on haematological parameters in albino rats

Physalis angulata leaves extract	Packed cell volume (%)	Red blood cell ($\times 10^6$ µL^{-1})	White blood cell ($\times 10^3$ µL^{-1})
50 mg kg^{-1}	48.2±1.1	18.1±0.7*	2.9±1.9
100 mg kg^{-1}	49.3±1.0	19.1±0.9*	2.7±2.9
200 mg kg^{-1}	50.1±0.8	21.0±1.0*	3.2±2.4
Control	44.7±1.2	15.1±1.0	3.0±2.1

Data are expressed as Mean±SEM, n = 6 and *Significant at p<0.05 when compared with the control

Table 2: Effect of *Physalis angulata* leaves ethanolic extract on biochemical parameters in albino rats

Physalis angulata leaves extract	Alanine transaminase (U L^{-1})	Aspartate transaminase (U L^{-1})	Creatinine (µmol L^{-1})	Cholesterol (mmol L^{-1})
50 mg kg^{-1}	28.8±1.2	72.0±1.2	23.0±1.6	6.0±1.5*
100 mg kg^{-1}	29.3±1.4	71.8±1.4	22.9±1.2	6.1±1.2*
200 mg kg^{-1}	29.8±1.2	72.1±1.3	22.8±1.5	6.2±0.9*
Control	30.0±1.0	72.4±1.2	22.8±1.9	9.8±1.1

Data are expressed as Mean±SEM, n = 6 and *Significant at p<0.05 when compared with the control

Effect of *Physalis angulata* leaves ethanolic extract on water (mL) intake: The plant extract caused no significant (p<0.05) change in water intake by albino rats when compared with the control (Fig. 3).

Effect of *Physalis angulata* leaves ethanolic extract on haematological parameters: The plant extract caused a significant (p<0.05) increase in the level of red blood cells and there was no significant (p<0.05) change in the level of packed cell volume and white blood cells of albino rats when compared with the control (Table 1). The increase in the level of red blood cells caused by the extract was dose-dependent (the higher the dose of the extract the higher the increase in red blood cells) (Table 1).

Effect of *Physalis angulata* leaves ethanolic extract on biochemical parameters: *Physalis angulata* leaves ethanolic extract caused no significant (p<0.05) change in serum alanine transaminase, aspartate transaminase and creatinine concentration when compared with the control in albino rats (Table 2). However, the plant extract caused a significant decrease in serum cholesterol levels when compared with the control (Table 2).

DISCUSSION

In this study, *Physalis angulata* leaves ethanolic extract exerted no toxic effect in the albino rats all through the study. In the acute toxicity study, the plant extract caused no signs of toxicity such as nausea, vomiting, diarrhoea, convulsion, mortality and changes in the skin, eyes and fur colour. The Median Lethal Dose (LD_{50}) of *Physalis angulata* leaves ethanolic extract was greater than or equal to 5000 mg kg^{-1} which suggested that the plant extract at the highest dose (5000 mg kg^{-1}) administered is not toxic after single oral administration to albino rats. A previous acute toxicity study carried out on *Physalis angulata* leaves methanolic extract reported that the plant extract caused no death at 2000 mg kg^{-1} [25]. A toxicity study carried out on the aqueous

extract of *Physalis angulata* root showed that 10-60 mg kg^{-1} of the extract administered to mice caused no behavioural changes such as sedative effect, respiratory depression and involuntary movement[26]. The study carried out by Bastos *et al.*[26] concluded that *Physalis angulata* root aqueous extract caused low acute toxicity. Alves *et al.*[27] determine the genotoxic effect of *Physalis angulata* aqueous extract on human lymphocytes using the *in vitro* model.

In the sub-chronic toxicity studies, *Physalis angulata* leaves ethanolic extract caused no significant ($p<0.05$) change in body weight (Fig. 1), food intake (Fig. 2) and water intake (Fig. 3) when compared with the control. In haematological parameters, the plant extract caused a significant ($p<0.05$) increase in the level of red blood cells in a dose-dependent manner and no changes in the level of packed cell volume and white blood cells when compared with the control (Table 1). The plant extract caused a significant ($p<0.05$) decrease in cholesterol concentration when compared with the control (Table 2). In toxicity studies, changes in body weight, food intake, water intake and haematological and biochemical parameters are determined to ascertain the safety and possible toxicity of some medicinal plants[20,28,29]. Haematological parameters which include the red blood cells count, white blood cells count and packed cells volume and biochemical parameters which include alanine transaminase, aspartate transaminase, creatinine and cholesterol are some of the indicators used to determine the toxicity and safety of a plant[30].

The results from this study showed that daily treatment of albino rats with *Physalis angulata* leaves ethanolic extract for twenty-one days caused no adverse effect on the body weight and haematological and biochemical parameters of the animals.

CONCLUSION

In conclusion, the results from this study suggested that *Physalis angulata* leaves ethanolic extract caused no toxic effect at the doses used for this study when orally administered to albino rats.

SIGNIFICANCE STATEMENT

This study discovered that *Physalis angulata* leaves ethanolic extract exerted no toxic effect on body weight, haematological parameters (red blood cell, white blood cell and packed cell volume) and biochemical parameters (alanine transaminase, aspartate transaminase, creatinine and cholesterol) in albino rats. This study will help researchers to carry out further pharmacological studies on *Physalis angulata* leaves using albino rats due to its safety levels (Median Lethal Dose [LD_{50}] was $\geq$5000 mg kg^{-1}).

REFERENCES

1. Osho, A., T. Adetunji, S.O. Fayemi and D.P. Moronkola, 2010. Antimicrobial activity of essential oils of *Physalis angulata* L. Afr. J. Traditional Complementary Altern. Med., 7: 303-306.
2. Silva, M.T.G., S.M. Simas, T.G.F.M. Batista, P. Cardarelli and T.C.B. Tomassini, 2005. Studies on antimicrobial activity, *in vitro*, of *Physalis angulata* L. (Solanaceae) fraction and physalin B bringing out the importance of assay determination. Mem. Inst. Oswaldo Cruz, 100: 779-782.
3. Hwang, J.K., J.S. Shim and J.Y. Chung, 2004. Anticariogenic activity of some tropical medicinal plants against *Streptococcus mutans*. Fitoterapia, 75: 596-598.
4. Soares, M.B.P., D. Brustolim, L.A. Santos, M.C. Bellintani and F.P. Paiva *et al.*, 2006. Physalins B, F and G, *seco*-steroids purified from *Physalis angulata* L., inhibit lymphocyte function and allogeneic transplant rejection. Int. Immunopharmacol., 6: 408-414.
5. Vieira, A.T., V. Pinho, L.B. Lepsch, C. Scavone and I.M. Ribeiro *et al.*, 2005. Mechanisms of the anti-inflammatory effects of the natural secosteroids physalins in a model of intestinal ischaemia and reperfusion injury. Br. J. Pharmacol., 146: 244-251.
6. Kuboyama, T., C. Tohda and K. Komatsu, 2005. Neuritic regeneration and synaptic reconstruction induced by withanolide A. Br. J. Pharmacol., 144: 961-971.
7. Choi, E.M. and J.K. Hwang, 2005. Effect of some medicinal plants on plasma antioxidant system and lipid levels in rats. Phytother. Res., 19: 382-386.
8. Abe, F., S. Nagafuji, M. Okawa and J. Kinjo, 2006. Trypanocidal constituents in plants 6. Minor withanolides from the aerial parts of *Physalis angulata*. Chem. Pharm. Bull., 54: 1226-1228.
9. Coelho-Ferreira, M., 2009. Medicinal knowledge and plant utilization in an Amazonian coastal community of Marudá, Pará State (Brazil). J. Ethnopharmacol., 126: 159-175.
10. Geissler, P.W., S.A. Harris, R.J. Prince, A. Olsen and R.A. Odhiambo *et al.*, 2002. Medicinal plants used by Luo mothers and children in Bondo District, Kenya. J. Ethnopharmacol., 83: 39-54.
11. Lawal, I.O., N.E. Uzokwe, A.B.I. Igboanugo, A.F. Adio and E.A. Awosan *et al.*, 2010. Ethno medicinal information on collation and identification of some medicinal plants in Research Institutes of South-West Nigeria. Afr. J. Pharm. Pharmacol., 4: 1-7.
12. Bourdy, G., S.J. De Walt, L.R. Chavez de Michel, A. Roca and E. Deharo *et al.*, 2000. Medicinal plants uses of the Tacana, an Amazonian Bolivian ethnic group. J. Ethnopharmacol., 70: 87-109.

13. Roosita, K., C.M. Kusharto, M. Sekiyama, Y. Fachrurozi and R. Ohtsuka, 2008. Medicinal plants used by the villagers of a Sundanese community in West Java, Indonesia. J. Ethnopharmacol., 115: 72-81.
14. Agra, M.F., G.S. Baracho, K. Nurit, I.J.L.D. Basílio and V.P.M. Coelho, 2007. Medicinal and poisonous diversity of the flora of "Cariri Paraibano", Brazil. J. Ethnopharmacol., 111: 383-395.
15. Reddy, C.S., K.N. Reddy, E.N. Murthy and V.S. Raju, 2009. Traditional medicinal plants in Seshachalam hills, Andhra Pradesh, India. J. Med. Plants Res., 3: 408-412.
16. Akendengue, B., 1992. Medicinal plants used by the Fang traditional healers in Equatorial Guinea. J. Ethnopharmacol., 37: 165-173.
17. Demain, A.L. and S. Sanchez, 2009. Microbial drug discovery: 80 years of progress. J. Antibiot., 62: 5-16.
18. Ekor, M., O.A. Osonuga, A.O. Odewabi, A.G. Bakre and K.S. Oritogun, 2010. Toxicity evaluation of yoyo 'cleanser' bitters and fields swedish bitters herbal preparations following sub-chronic administration in rats. Am. J. Pharmacol. Toxicol., 5: 159-166.
19. Ekor, M., 2014. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. Front. Pharmacol., Vol. 4. 10.3389/fphar.2013.00177.
20. Sunday, R.M., O.R. Ilesanmi and E.M. Obuotor, 2016. Acute and sub-chronic oral toxicity of anthocleista vogelii (cabbage tree) root hydroethanolic extract in albino rats. J. Pharm. Res. Int., Vol. 12. 10.9734/bjpr/2016/27018.
21. Lorke, D., 1983. A new approach to practical acute toxicity testing. Arch. Toxicol., 54: 275-287.
22. Huang, X.J., Y.K. Choi, H.S. Im, O. Yarimaga, E. Yoon and H.S. Kim, 2006. Aspartate aminotransferase (AST/GOT) and alanine aminotransferase (ALT/GPT) detection techniques. Sensors, 6: 756-782.
23. Bartels, H., M. Bohmer and C. Heierli, 1972. Serum kreatininbestimmung ohne enteiweissen. Clin. Chim. Acta, 37: 193-197.
24. Richmond, W., 1992. Analytical reviews in clinical biochemistry: The quantitative analysis of cholesterol. Ann. Clin. Biochem., 29: 577-597.
25. Rathore, C., K.R. Dutt, S. Sahu and L. Deb, 2011. Antiasthmatic activity of the methanolic extract of *Physalis angulata* Linn. J. Med. Plants Res., 5: 5351-5355.
26. Bastos, G.N.T., A.R.S. Santos, V.M.M. Ferreira, A.M.R. Costa, C.I. Bispo, A.J.A. Silveira and J.L.M. do Nascimento, 2006. Antinociceptive effect of the aqueous extract obtained from roots of *Physalis angulata* L. on mice. J. Ethnopharmacol., 103: 241-245.
27. dos Santos, R.A., T.R. Cabral, I.R. Cabral, L.M.G. Antunes and C.P. Andrade *et al*., 2008. Genotoxic effect of *Physalis angulata* L. (Solanaceae) extract on human lymphocytes treated *in vitro*. Biocell, 32: 195-200.
28. Oduola, T., I. Bello, G. Adeosun, A.W. Ademosun, G. Raheem and G. Avwioro, 2010. Hepatotoxicity and nephrotoxicity evaluation in Wistar albino rats exposed to *Morinda lucida* leaf extract. North Am. J. Med. Sci., 2: 230-233.
29. Sunday, R.M., O.R. Ilesanmi and E.M. Obuotor, 2013. Acute and subacute toxicity of aqueous extract of abrus precatorius seed in Wister rats. Internet J. Pharmacol., Vol. 11. 10.5580/2ce3.
30. Olayode, O.A., M.O. Daniyan and G. Olayiwola, 2020. Biochemical, hematological and histopathological evaluation of the toxicity potential of the leaf extract of *Stachytarpheta cayennensis* in rats. J. Traditional Complementary Med., 10: 544-554.