INTRODUCTION

The vascular endothelium is important in the regulation of vascular haemostasis; its alteration has also been suggested to contribute to the pathogenesis of cardiovascular diseases [1]. Platelet aggregation plays a central role in coronary thrombosis and also contributes to the development of atherosclerosis [2]. A blood clot is depended on the balance between pro-coagulants and anticoagulants in the bloodstream. The anticoagulant predominates when a vessel is ruptured while pro-coagulants from the area of tissue damage become activated and override the anticoagulant; thus, clots do not develop [3, 4]. Several studies have reported the effect of specific beverages and foods on inhibiting platelet aggregation, whereas limited works have been reported on beverages and foods stimulating platelet aggregation [5]. Thus, a diet rich in natural platelet stimulato rs or inhibitors may determine an individual's risk of developing cardiovascular disorders.

Onion is the term used for many plants in the genus "Allum" but usually refers to Allium cepa. It is known only in cultivation; however, related species occur in central Asia [6]. Onion is utilized globally in culinary practice due to its unique flavours in foods that range from very mild to pungent form [7]. It is the second most important crop after tomato. Global production of about 66 million tonnes is achieved annually [8]. Onion contains an organic sulphur compound, phenolic acid, flavonoids, sterols, the trace of volatile oil, vitamin C, vitamin B6 and trace elements [9, 10]. Researchers have shown its wide pharmacological applications in the treatment of cancer, inflammation, asthma, oxidative stress, cardiovascular diseases and other health conditions [4, 11-13]. In addition to these, several works have also investigated the haemostatic effect of some onion varieties. However, there are conflicting views on the role of different onion varieties and genotypes on both platelet aggregation and anti-platelet activities using different models [4, 14-19]. Thus, identification of the varieties with better health benefits is essential in curbing some diet-induced functional and morphological distortions in tissues.

The present study investigated the effect of aqueous extract of Brown Onion (Allium cepaL) on bleeding, clotting time and differential platelet count of Wistar albino rats.

MATERIALS AND METHODS

Drugs and chemicals

All reagents utilized for this study were of analytical grade; Methylated Spirits (Sigma Aldrich Company Ltd, Dorset England), Filter Papers (Rippert and Anlagentechnik GMBH and CO. KG, Herzebrock-clarholz, Germany) Giemsa stain (Sigma Aldrich Company Ltd, Dorset England).

Plant samples collection, identification and extractions

Fresh brown onions were obtained from samaru market, Zaria, Kaduna state, Nigeria. Identification was done at the herbarium unit of Biological Sciences Department, Ahmadu Bello University, Zaria, Nigeria. The voucher number is 2196. The outermost layer was removed and the onions were sliced using a knife. The sliced onion was put into a blending machine and crushed into a watery paste. Water was added during this process. The onion juice was left for an hour after which it was decanted into an evaporating dish. The evaporating dish was placed into a water bath and heated at 40 degrees Celsius during which there was evaporation from the onion juice. The evaporating dish was left with the concentrated extract. The whole process lasted for 3 d.

Acute toxicity (LD50) test

The mean lethal dose of aqueous Allium cepaL was determined in albino rats using the intraperitoneal route as described by Lorke [20]. The LD50 was found to be 1264.9 mg/kg.

Experimental animals

A total of sixteen albino rats of male sex, weighing 140-180g were purchased from the faculty of Pharmaceutical sciences, Ahmadu Bello University, Zaria, Nigeria. The animals were housed in steel wire cages in a room where the congenital temperature was 27 ±1 °C and 12 h light and dark cycles were maintained. The animals were allowed to acclimatized to the environment for two weeks and supplied with a standard pellet diet and water ad libitum. The study was conducted in accordance with the Ethical Committee Guidelines of the institution on the use of animals for research.

OBJECTIVE

The study investigated changes in haemostatic parameters such as; bleeding time, blood clotting time and differential platelet counts of wistar rats following repeated administration of aqueous extract of allium cepa L.

METHODS

Rats were divided into four groups of four animals each (n=4). Group I served as normal control, Group II, group III and group IV were administered 25 mg/kg bw, 50 mg/kg bw and 100 mg/kg bw of the extract intra-peritoneally for two weeks, respectively. After 14 d experimental period, blood samples were collected for the determination of bleeding time, clotting time and differential platelet count.

RESULTS

The findings of this study revealed a significantly increased (p<0.05) clotting time at a dose of 25 mg/kg but showed no significant change in bleeding time and differential platelet count of all the groups.

CONCLUSION

Aqueous extract of brown onion showed anti haemostatic effect in albino rats by increasing clotting time at a lower dose.

KEYWORDS: Bleeding time, Clotting time, Allium cepa, Haemostasis, Rats

ABSTRACT

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Original Article

CHANGES IN HAEMOSTATIC PARAMETERS OF WISTAR RATS FOLLOWING REPEATED ADMINISTRATION OF AQUEOUS EXTRACT OF BROWN ONION (ALLUMCEPAL)

ZUBERU JIBRIL1, SANI SANUSI2

1BM Diagnostic Services, Kaura Namoda Zamfara State, 2Medical Services Department Federal Polytechnic Kaura Namoda Zamfara State

Email: Abdullahizubairu13@gmail.com

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Animal groupings
The rats were randomly divided into 4 groups of 4 rats each.

Group I: Normal control received feed and distilled water only for 14 d.
Group II: Normal rats treated with aqueous extract of *Allium cepa* L. 25 mg/kg bw/day intraperitoneally for 14 d.
Group III: Normal rats treated with aqueous extract of *Allium cepa* L. 50 mg/kg bw/day intraperitoneally for 14 d. Group IV: Normal rats treated with aqueous extract of *Allium cepa* L. 100 mg/kg bw/day intraperitoneally for 14 d.

Determination of bleeding time
Using the method of Dukes [21], the tail end of the rats was disinfected using a methylated spirit. A scissors was used to cut the tail. The bleeding time of the rats was done by counting the number of spots that blotted on filter paper, multiplied by the number of interval that blotted on the filter paper and divided by 60 seconds.

Determination of clotting time
Clotting Time was calculated as described by Lee and White [22]; Briefly, the tails of the animals from each group were cleaned and disinfected with methylated spirit, then cut with scissors. The tip of the tail of each animal was immediately directed into four plain glass test tubes. 1 ml of blood was taken from the animal and immediately delivered into 4 clean test tubes (75 x 10 mm) already standing in a turn every 30 seconds until tilted through an angle greater than 90˚ without spillage. The electronic stopwatch was started immediately blood starts oozing out of the animal into the test tubes. The average time was then calculated for clotting.

Determination of platelets counts
The method used is known as Differential count method. Briefly, drops of blood were collected on slides and used to prepare smear. The smear was fixed in methyalcohol for 3 min. Staining of the slides was done using Giemsa dilution for 20 min. The slides were rinsed using water and then with a buffer of P.H 7.0. Counting of the different types of platelets was determined using an amsalco electronic microscope [23].

Statistical analysis
Data obtained were expressed as mean (±SEM). The result was analysed using one way analysis of Variance(ANOVA), followed by an appropriate post-hoc test to compare the level of significance between groups using SPSS version 17.0. Values of p<0.05 was considered significant.

RESULTS
Effect of aqueous extract of brown onion on bleeding time of albino rats
There was no statistical significant difference (p>0.05) between the normal control group and all the treated groups as shown in fig. 1.

Effect of aqueous extract of brown onion on clotting time of albino rats
There was a significant increase (p<0.05) in clotting time of group treated with 25 mg/kg of the onion extract when compared to the normal control group (1.27±0.04 min), as shown in fig. 2. The mean clotting time of the treated group at 25 mg/kg (2.57±0.16 min) was significantly increased compared to groups treated with 50 mg/kg (1.35±0.07 min) and 100 mg/kg (0.95±0.15 min) of the extract, respectively.

Effect of aqueous extract of brown onion on differential platelet count of albino rats
There was no statistical significant difference (p>0.05) between the normal control group and all the treated groups, as shown in table 1.
DISCUSSION

Haemostasis is a fundamental and complex defence mechanism of all vertebrates. The process of haemostasis requires multiple interdependent interactions between platelets, endothelial cells, white cells and plasma proteins [24]. Blood normally remains in the liquid state while it is within the blood vessels, but when it leaves the vessels, the blood may thicken and form a gel and subsequently transform into a solid state. It is one of the three mechanisms in haemostasis which denotes the cessation of blood loss from a damaged vessel [4]. Platelets are essential during haemostatic process; when they are activated during endothelial cells damage, platelets aggregate, and adhere to the lining of arteries [17, 25]. Following a break in the endothelial lining, there is an initial adherence of platelets to exposed connective tissue which is potentiated by von Willbrand factor (VWF). Platelets begin to aggregate minutes after activation as a result of turning on the glycoprotein lib/IIia receptors which will in turn bind to von Willbrand factor [26]. Collagen exposure and thrombin produced at the site of injury cause the adherent platelets to release their granule contents and also activate platelet prostaglandin synthesis, leading to the formation of thromboxane A2 [27]. Releasing Adenosine Diphosphate (ADP) causes platelets to swell and aggregate. Additional platelets from the circulating blood are drawn to the area of injury. This continuing platelet aggregation promotes the growth of the haemostatic plug which soon covers the exposed connective tissue [4, 27]. However, hyperactivity of platelets can contribute to artherosclerosis formation, coronary syndrome, peripheral vascular diseases, stroke and thrombosis [17, 25]. The present study was carried out to determine the potentials of brown onion variety on the haemostatic mechanism of albino rats, with primary interest being how it affects bleeding, clotting time and differential platelet counts respectively. From the results above, there was a significant increase in clotting time with the tendencies to also increase bleeding time at 25 mg/kg (table 1). A previous study using the same variety of allium cepa L. to determine its effects on clotting time on pigs yielded small but insignificant result with platelet number unaffected [28]. Chen et al.[15] reported from their study that onion prolonged bleeding time, diminished platelet adhesion on fibrinogen coated surface ADP evoked platelet aggregation, ADP stimulated thromboxane release, elevated cyclic AMP in platelet sand increased the plasma level of 6-keto-prostaglandin F. Compounds that have been implicated in providing a number of health promoting attributes of onions include flavonoids, particularly the quercetin and organosulphur compound such cysteine sulphoxide [29]. The number of quercetin and phenolic compounds present in onion skin are up to 5 times higher than the edible part [9]. The inhibitory effect of dietary flavonoids on platelet function has been recognized for some time, with recent reports showing the identity of specific targets of collagen mediated signalling pathways that leads to platelets activation, are inhibited by quercetin in vitro. This includes Src-family kinases, tyrosine kinase and phosphoinositide-3-kinase [31]. Despite these effects, there are mixed results documented concerning the effect of flavonoids in anti-inflammatory and cardiovascular risk [1]. Also, research work carried out to determine whether all onion varieties have natural anti-thrombotic effect as assessed by thrombosis/thrombolysis models in rodents, showed that allium cepa can be classified into varieties; with or without anti-thrombotic activity [19]. The ability of brown onion to increase both bleeding and clotting time from our study may be due to its active ingredients with a direct or indirect effect on the clotting cascade as it correlates to the study of Chen et al.[15]. Also observed from this study, is dose-dependent decrease is bleeding and clotting time (fig 1 and 2).

Hence, aqueous brown onion extract may decrease bleeding and clotting time at higher doses. There was no significant difference in the differential platelet count of wistar rats after repeated administration of aqueous onion extract (table 1). Our results contradict the findings of Ro et al.[17], but may align with the findings of Ewaet al.[28] and Meraiyebet al.[32]. This difference may be attributed to the onion variety [33], the percentage composition of active ingredients, geographical distribution and study design. While in vitro effect of aqueous extract of onion on collagen-induced platelet aggregation using rabbit and human platelet-rich plasma, resulted in dose-dependent inhibitory effects on collagen-induced platelets [34], in vitro incubation of onion juice demonstrated that platelet inhibitory response was significantly greater than in human blood [2]. The effect of onion in vitro platelet activity was reported to be time-dependent [35].

CONCLUSION

Aqueous extract of brown onion variety (allium cepa L.) possessed anti haemostatic property at a low dose (25 mg/kg). This is evidenced by a significant increase in clotting time of albino rats following repeated administration. People with bleeding disorders are therefore advised to reduce the consumption of brown onion. Phytochemical studies and isolation of active ingredients of this onion variety may help in evaluating its potential health hazards and/or benefits.

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Nil

AUTHORS CONTRIBUTIONS

Research design and analysis were done by Jibril Zuberu while Sanusi Sani discussed the results and made recommendations.

CONFLICT OF INTERESTS

Authors have declared that no competing interests exist.

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Table 1: Effect of aqueous extract of brown onion (allium cepa L.) on differential platelet count of albino rats

| Groups (n=4) | NP/100 | AP/100 | FP/100 | PA/100 |
|-------------|--------|--------|--------|--------|
| Normal      | 19.50±1.47 | 19.50±2.66 | 18.50±1.37 | 18.50±1.93 |
| 0.00 mg/kg  | 19.50±2.66 | 18.50±1.80 | 17.50±1.55 | 18.50±2.03 |
| 1.00 mg/kg  | 19.50±1.38 | 18.50±1.50 | 17.50±1.49 | 18.50±1.90 |
| 2.50 mg/kg  | 19.50±1.80 | 18.50±2.00 | 17.50±1.35 | 18.50±2.00 |
| 5.00 mg/kg  | 19.50±2.00 | 18.50±2.20 | 17.50±1.30 | 18.50±2.00 |

‘Results are expressed as mean±standard error of mean n = 5. NC: Normal Control AC: allium cepaL. NP: Normal Platelet, AP: Aggregated Platelets, FP: Filamentous Platelet, PA: Platelets Anisocytosis. No statistical significance between all the group (p>0.05).
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