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Research Article

Human in vivo study: The Effect of Gum Arabic on Coagulation Cascade

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Abstract: Recent researches demonstrate the biological activity of Gum Arabic (GA) and promote the use of GA in medicine. This study was designed to determine the effect of GA on human coagulation system. A pilot study was set out. A total of 47females were enrolled in the study and divided into two groups, randomly, a control with 18 females and intervention group with 29 females. A dose of 30g/ day/ 8 weeks of GA, was administrated to the intervention group .Blood samples were collected pre and post intervention and Prothrombin time (PT) and Activated Partial Thromboplastin Time (APTT) were estimated and compared to controls. Results revealed that, the mean difference of the PT in seconds of the intervention group was (1.02 ± 0.31) and differ significantly from the control group (-0.33 ± 0.29).Whilst the mean difference value of APTT in seconds of the intervention group was (-1.9 ± 0.69) and not significantly increased in comparison to the control (-0.94 ± 0.98) group. This study established GA anticoagulant effect in human and nominated GA as potential preventive agent for thromboembolic diseases. While more studies are needed to demonstrate the curative effectiveness.

Key words: Gum Arabic, coagulation, humans, anticoagulant, Activated Partial Thromboplastin Time (APTT), Prothrombin Time (PT).

INTRODUCTION

Gum Arabic (GA) is the dried, gummy exudate from the stems and branches of Acacia Senegal and Acacia Seyal[1]. GA is a branch-chain, complex polysaccharide, found as mixed calcium, magnesium and potassium salt of Arabic acid [2]. Gum Arabic has many uses in industries including soft drinks, textile, pottery, cosmetics and pharmaceutical industries as stabilizer , thickening agent and emulsifier[3].

In the past GA was considered as an inert substance with no pharmacological effect on the living systems, but all recent research changed this concept and GA now had many useful uses in the medical field[4]. GA demonstrate a prebiotic effect in human in a dose dependent manner, this effect is indicted by the increase in the numbers of the Bifidobacteria and Lactobacilli.[5] GA cannot be degraded in the stomach and small intestine, but undergone complete fermentation within the humans cecum[6]. This promoted the production of the short chain fatty acids (SCFAs) by colonic bacteria[7]. The major SCFAs produced by fermentation were acetate, propionate and butyrate[8].

Most of the systemic effects of the GA are attribute to fermentation products.GA preliminary studies in rats demonstrate these biological effect .Propionate act as gluconeogenic substrate reducing amino acid consumption and in turn urea formation[7, 8]. Beside that antioxidant[9, 10], hypoglycaemic[11, 12] and immunomodulatory effect are reported[13, 14].GA has anticoagulant effect demonstrated by prolongation in the bleeding time (BT) and prothrombin time (PT) in Wistar rats, where activated partial thromboplastin time (APTT) is not affected[15].

In man GA is suggested as alternative approach to treat renal failure due to the urea lowering effect and promotion of urea excretion in the faeces [16].Ingestion of GA cause significant reduction in low density lipoprotein (LDL) and very low density lipoprotein (VLDL), body mass index (BMI) and body fat percentage and nominate GA as possible treatment for obesity[17, 18]. Although experimental animal data were available regard GA anticoagulant effect in rats[15], no human data was reported. This study was set out to investigate whether GA affect human coagulation cascade or not

EXPERIMENTAL SECTION

Ethical considerations

The study protocol has been approved by institutional ethical committee of faculty of medicine, Khartoum University. While all Subjects were recruited voluntary after taking written informed consent.

Study design

All the enrolled participants were healthy medical female student, aged between 18-19 years old. They were non-smoker, not on regular exercise or on controlled diet.

A total of 47 participants were randomly assigned in two groups, a control with 18 subjects and intervention with 29 subjects. During the study period of 8 weeks,30mg/day of commercial gum Arabic powder of Acacia Senegal (Dar Savanna, Sudan) have been given orally to the member of the intervention group while the control group members did not receive any thing.

Sample preparation

3ml of venous blood sample was collected from the volunteers' brachial vein using citrate vacuutainersat the beginning and the end of the study period. Samples were centrifuged at 3000 RPM for 10 minutes. Then plasma aliquots were collected in plain containerand stored in the refrigerator at -30c^{o}until assayed within 10 days.

Parameters estimation

A. Prothrombin Time

PT was estimated using High Sensitive Prothrombin Time Reagent (Fortress diagnostic-England). 100 µL of the plasma aliquots were placed into plain glass test tube then rapidly 200 µL of PT regent (incubated at 37^{o} for 10 minutes, and mixed by inversion to homogenize)were added, and PTin seconds was recorded immediately.

B. Activated Partial Thromboplastin Time

APTT was estimated using Activated Partial Thrombplastin Time Regent (Fortress diagnostic-England). 100 µL of the plasma aliquots were placed into plain glass test tube and incubated for 1-2 minutes at 37^{o}C, then 100 µL of the APTT reagent were added to the test tube and the mixture was incubated for 3 minutes.100 µL of the calcium chloride solution (0.02 M), pre- incubated at 37^{o}C for 10 minutes, were added and the APPTin seconds was recorded immediately.

Data analysis

Data were analysed using Graph pad prism version 5.Data were compared by unpaired t-test and considered significant at p-value level ≤ 0.05.

RESULTS AND DISCUSSION

Both of PT and APTT pre and post intervention among the test group showed significant difference, see table 1. The mean differences (Mean ± S.E.M) calculated from the estimated values of PT and APTT for both groups before and after the GA administration were presented in table 2.

The PT has shown prominent increase among the test group in comparison to the control during the study period of 8 weeks, see Figure 1. Moreover the APTT exhibited consistent reduction among the two groups in similar manner with no significant difference, see figure 2.

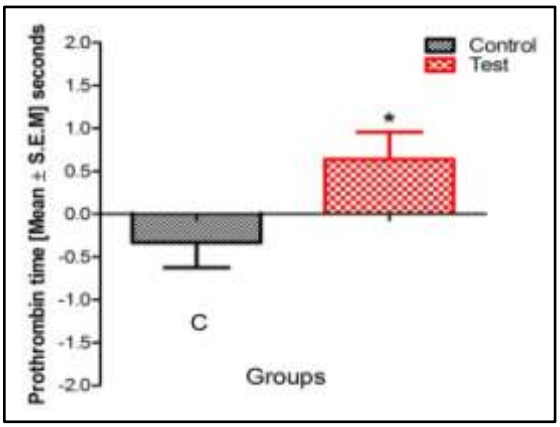

Fig. 1: comparison between control and test PT mean difference, Values presented are means of (18 or 29 volunteers) for control and test group, respectively, vertical bar donates standard error of mean (S.E.M.), * P ≤ 0.05.

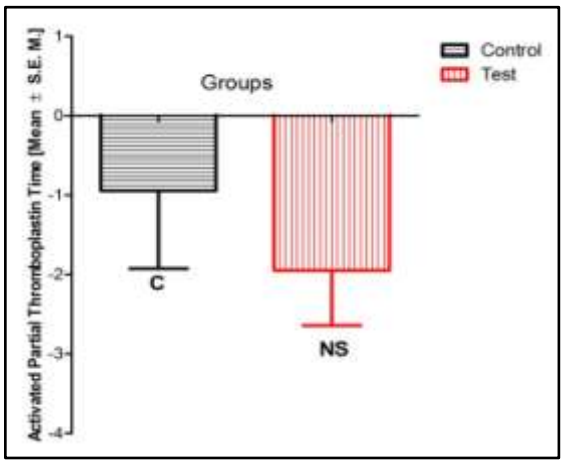

Fig. 2: comparison between control and test APTT mean difference, presented are means of (18 or 29 volunteers) for control and test group, respectively, vertical bar donates standard error of mean (S.E.M.)NS: not significant.

Table-1: The PT and APTT mean values (Mean ±S.E.M.)at the start and end of the study period for the test and control in seconds.

Parameters	**Control** (n=18)		**Test** (n=29)	
	Before	*after*	*before*	*after*
PT	13.7± 0.2	13.3±0.2	13.7±0.2	14.3±0.2*
APTT	27.2 ± 0.7	26.3±0.6	27.9 ± 0.4	26.0±0.5**

PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time.* P ≤ 0.05, ** P ≤ 0.01.

Table 2: PT and APPT mean difference among test and control in seconds including outliers

Parameters	(Mean ± S.E.M.)	
	PT(n=29)	**APTT(n=29)**
Control (n=18)	-0.33± 0.29	-0.94 ± 0.98
Test	0.64 ± 0.32	-1.95 ± 0.69
p-value	0.016	0.395

PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time.

It is well known that oral anticoagulants have limitations, which restricted their use, thus safe efficient new anticoagulant is highly recommended.GA was nominated due to the promising in vitro data in rats.

Since the study participants were the medical student and the majority of them were females, whom were more expected to be susceptible to develop thromboembolic disorders[19], hence our study subjects were selected exclusively from female students.

Our findings revealed that the blood coagulation investigated parameter PT was increased significantly, indicating the presence of substance that possess direct or indirect effect on normal coagulation process which in line with Abdul-Hadi et.al.(2010)findings in rats, regarding the PT and APTT which was not increased significantly.[15].

On the other hands, all the observed parameters changes were within the normal physiological range for both PT and APTT, this indicate reasonable margin of safety that enable it to take place in clinical practice as a preventive agent for coagulation disorders which were associated with high morbidity and mortality rate worldwide[19]. These results indicated that GA effect is mainly with in the extrinsic coagulation pathways.

The GA modulation effects at the extrinsic pathway may be attributed to the fermented metabolite of GA (acetate, propionate and butyrate).Veldeman et.al. reported that pectin oral administration in hyperlipidemic subjects affected fibrin network and the conversion of fibrinogen to fibrin, the network became more permeable and lyseable and the action is partially related to the fermentation product, acetate[20]. This can support the theoretical mechanism of action of GA and indicted that the influence of fermentation products is on multiple target with in the coagulation cascade.

CONCLUSION

It can be concluded that, GA chronic use show an increase in PT within the normal physiological level, promoting GA safety. The extrinsic coagulation pathway was affected, and acetate is proposed in mediating this potential effect. GA can be regarded as mild strength anticoagulant, that can take a place as useful natural anticoagulant for prevention with no tendency to cause bleeding ,while the curative property of GA is a hot research area and more efforts are needed to confirm its effectiveness and to postulate the exact mechanism of action.

Conflict of interests

None

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