**Revue Agrobiologia**
www.agrobiologia.net
ISSN (Print): 2170-1652
e-ISSN (Online): 2507-7627

# EFFECT OF ADMINISTRATION OF GINSENG SOLUTION *PANAX GINSENG* ONBLOOD COAGULATION PARAMETERS AMONG A POPULATION OF MICE (*MUS MUSCULUS*)

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*Reçu le 25/12/2021, Révisé le 22/04/2022, Accepté le 23/04/2022*

## Abstract

**Topic Description:** The anticoagulant potential of some medicinal plants such as *Panax ginseng* is attracting the interest of many studies
**Objectives:** The current study aims to investigate the anticoagulant potential of *Panax ginseng in vitro*.
**Methods:** We assessed and compared variations in platelet levels, prothrombin time, and activated partial thromboplastic time in 68 *Mus musculus* mice divided into three groups: force-fed with *Panax notoginseng* distilled water, and rice flour (450mg/kg).
**Results:** Our results showed a significant prolongation of the activated partial thromboplastin time following prolonged force-feeding with *Panax ginseng* solution: AtT0 13.6±1.3 sec vs 22.6±1.5 sec (Z Wilcoxon=-4.19 / $p$ <0.01) at the end of the force-feeding period. The active prothrombin time was 12.5 sec at the beginning of the experiment and 20.45 sec after 45 days of ginseng gavage (Wilcoxon=-4.27 / $p$<0.01).Furthermore, the platelet count did not differ significantly across all groups or over the course of the experiment (Z Wilkoxon=-4.14 / $p$=0.11).
**Conclusion:** This study concluded that *Panax ginseng* has a strong anticoagulant potential. Further research into the antiplatelet potential of *Panax ginseng* should be conducted using other biological indicators, specifically the effect of Ginseng on platelet functions.
**Keywords:** Ginseng, Blood coagulation, Mice, Anticoagulant Proprieties, antiplatelet agent

# EFFET DE L'ADMINISTRATION DE LA SOLUTION DE *PANAX GINSENG* SUR LES PARAMÈTRES DE LA COAGULATION SANGUINE CHEZ UNE POPULATION DE SOURIS (*MUS MUSCULUS*)

## Résumé

**Description du sujet :** Le potentiel anticoagulant de quelques plantes médicinales tel que le *Panax ginseng* suscite l'intérêt de nombreuses études
**Objectifs :** L'étude actuelle vise à étudier le potentiel anticoagulant du *Panax ginseng in vitro*
**Méthodes :** Nous avons évalué et comparé les variations des taux de plaquettes, du temps de prothrombine et du temps de thromboplastie partielle activée chez 68 souris *Mus musculus* divisées en trois groupes : gavées à l'eau distillée, de *Panax notoginseng* et de farine de riz (450mg/kg).
**Résultats :** Nos résultats ont montré une prolongation significative du temps de thromboplastine partielle activée après un gavage prolongé avec une solution de Panax ginseng : AtT0 13,6±1,3 sec vs 22.6±1.5 sec (Z Wilcoxon=-4,19 / $p$ <0,01) à la fin de la période de gavage. Le temps de prothrombine active était de 12,5 sec au début de l'expérience et de 20,45 sec après 45 jours de gavage au ginseng (Wilcoxon=-4,27 / $p$<0,01). De plus, la numération plaquettaire ne différait pas significativement dans tous les groupes ou au cours de l'expérience (Z Wilkoxon=-4,14 / $p$=0,11).
**Conclusion :** Cette étude a conclu que le *Panax ginseng* a un fort potentiel anticoagulant. D'autres recherches sur le potentiel antiplaquettaire du *Panax ginseng* devraient être menées en utilisant d'autres indicateurs biologiques, notamment l'effet du Ginseng sur les fonctions plaquettaires.
**Mots clés:** Ginseng, coagulation sanguine, souris, propriétés anticoagulantes, agent antiplaquettaire

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## INTRODUCTION

Numerous studies on the therapeutic properties of medicinal plants have been conducted in recent years [1]. Ginseng is a medicinal plant in the Araliaceae botanical family [2], known for its therapeutic potential against a variety of diseases, including pleiotropic beneficial effects on the cardiovascular system [1, 3], central nervous system [3, 4], diabetes prevention, and immune system [3, 5]. Ginseng, specifically *Panax ginseng*, has also been linked to anticoagulant properties [5, 6, and 7] and is sometimes recommended as a way to improve the comfort of patients taking anticoagulants [8]. However, its mechanism of action on the coagulation cascade remains highly debated in this regard [9]. Few *in-vitro* studies have been conducted to determine which coagulation pathways (intrinsic or extrinsic) are influenced by ginseng-based treatments [2, 3]. According to other authors, this anticoagulant potential is primarily associated with an anti-platelet aggregation effects [6, 7, 10 and 11]. Following this bath, our study aimed to investigate the effect of Ginseng administration on the coagulation process by analyzing the evolution of intrinsic and extrinsicafter forced-feeding of *Panax ginseng.*

## MATERIEL AND METHODS

### *1. Experimental study*

The study's experimental protocol adheres to the National Committee for Research Ethics in Science and Technology's ethical guidelines for the use of animals in research [12].

The ginseng solution was obtained by homogenizing the powder root part of the *Panax Ginseng*plant with distilled water. The panax ginseng sample used is packaged and marketed in Algeria and comes from the cultures of Changbai Mountain area in the Northeast Chinese provinces of Heilongjiang, Jilin and Liaoning. After grinding to a fine particles size only less than 1.5 mm were saved, the powder was homogenized for 35 minutes at 25°C using a magnetic stirrer. To avoid clogging the feeding probe, all solutions (rice flour and Ginseng solution) were filtered with wattman paper and stored between 4 and 6°C. Ginseng and rice flour were administered at a dose of 450 mg/kg.

Our sample study began with 70 male mice (*Mus musculus*) delivered by the animal Department of the Pasteur Institute of Algeria, which two of them died before the experiment began, their average weight in males was 33.1 g [30-36 gr] against 29.5 g [26-32 gr] in females . The 68 male mice used in this study were divided into three groups: *(i)* Group 1, control group of 22 mice was force-fed with distilled water. *(ii)* Group 2, the 23 mice were force-fed with rice flour depleted in minerals and vitamins. *(iii)* Group 3, 23 mice were force-fed with ginseng solution. All the solutions were administered one day over two. The feeding probe used is reusable and made of stainless steel (Instech Laboratories, Inc. 22Ga) (0.5×0.9 mm). After each use, the probes are cleaned and sterilized. Blood samples were collected at ESSAIA in Algiers using two methods: the first via the retro-orbital sinus and the second via the mandibular vein over a ten-day period, from May 10 to June 21, 2021. T0: at the beginning of the experiment, T1: after 15 days of the first sampling, T2: after one month of the first sampling, and T3: after 45 days of the beginning of the experiment.

The following coagulation parameters were measured: thrombocytes, prothrombin time (TP), and activated cephalin time (ACT) (TCA). Prothrombin time is a semi-global coagulation test that allows for the *ex vivo* investigation of factors in the tissue factor pathway, also known as the extrinsic coagulation pathway (factors VII, X, V, II, and fibrinogen) [13]. It was determined after centrifuging the sample for 10 minutes at 4000 rpm in citrated tubes containing excess tissue factor (thromboplastin) and $Ca^{++}$ [14, 15]. However, the activated cephalin time (TCA) was measured in the presence of a phospholipid suspension, an activator (Kaolin), and calcium [16]. At the Central Laboratory of Biochimie, thrombocytes were counted using a hematological counter (CHU Mustapha Bacha, Algiers).

### *2. Statistical analysis*

The data was entered into an excel spreadsheet and analyzed with SPSS version 22 statistical software. The Kolmogorov Smirnov testis used to investigate the distribution of variables. All variables presented as medians and interquartile ranges. The Wilcoxon Comparison Test used to perform a comparative analysis on paired samples. However, after using a non-exhaustive comparative analysis Kruskal Wallis H test, a post hoc Mann-Whitney U test comparison performed for the independent samples. If the obtained P is less than 0.05, the probability is considered significant.

## RESULTS

The statistical analysis revealed that the distribution of thrombocyte values in the control group was significantly different from the Gaussian curve (KS=0.245; $p$<0.05). The variable's descriptive study revealed that at T0, the median was 561.24.30 $\times10^3$ /mm$^3$ [CI95 %: 561.45; 594.47]. Its values ranged from 557 to 660.9 $10^3$ /mm$^3$. The median at T1 was 558.16.1 $\times10^3$ /mm$^3$ / L [CI 95 %: 551.03; 571.47]. T2 and T3 showed slight variations, with values of 551.28.3$\times10^3$ /mm$^3$ [CI95 %: 556.84; 566.24] and 547.316$\times10^3$ /mm3 [CI95 percent: 546.85; 559.23]. In groups 2 and 3, the distribution pattern of all thrombocyte values (at T2, T3) was significantly different from a normal distribution, as compared to the control group (Table 1). The median values of thrombocytes in group 2 showed low variations between the start of force-feeding and the end of the experiment, with 560.225$\times10^3$ /mm$^3$ [CI95 %: 558.31 ; 560.41] at T0 and 54716$\times10^3$ /mm$^3$ [CI95 %: 516.67-548.93] at T3. The same observation was signaled for the group 3, where the amount of thrombocyte little bitvaried, with a median value of 569.168.13$\times10^3$/mm$^3$ at T0 and 527.24$\times10^3$/mm$^3$ at T3.

When we analyzed the activated partial thromboplastin time values, in both control groups 1 and 2 we did not find a remarkable variations between through the period of experiment. The median values for group 1 were 13.151.15 sec [CI95 %: 12.77; 13.39] at T0, and 13.30.955 sec [CI95 %:12.88-13.42] after 45 days of force-feeding. In comparison to the control group, the activated partial thromboplastin time values of group 2 did not vary, with a median value at the end of the experiment equal to 12.850.92 sec [CI95 %: 12,60-13.12] versus 12.801.20 sec [CI95 %: 12.52-13.11] at the start. However, in group 3 the median values of activated partial thromboplastin time were gradually lengthened as the period of force-feeding is longer, with: 12.51.55sec [CI95 % :12.50 ; 13.12] at T0, 16.11.6 sec [CI9 %: 15.53-16.5] at T1, 17.71.53 sec [CI95 %: 17.44-18.20] at T2, and 20.454 sec [CI95 % : 19.81-2197] (Table 1).

Table 1: Descriptive Study of Blood coagulation parameters

| **Parameters** | T0 | | T1 | | T2 | | T3 | |
|---|---|---|---|---|---|---|---|---|
| | Median±IQR | K.S/*p* | Median±IQR | K.S/*p* | Median±IQR | K.S/*p* | Median±IQR | K.S/*p* |
| ***Thrombocytes ×10³/mm³*** | | | | | | | | |
| Group 1(22) | 561±4.30 | 0.24/0.01 | 558.1±6.1 | 0.42/0.02 | 551.2±8.3 | 0.36/0.01 | 547.18±16 | 0.39/001 |
| Group 2(23) | 560.2±25 | 0.23/0.01 | 557.7±3.1 | 0.15/0.19 | 544±55 | 0.14/0.02 | 547.1±16 | 0.13/0.02 |
| Group 3(23) | 569.1±68 | 0.14/0.2 | 543.2±62 | 0.20/0.01 | 538±57.1 | 0.18/0.04 | 527.2±24 | 0.26/0.01 |
| ***TCA (seconds)*** | | | | | | | | |
| Group1 | 13.15±1.15 | 0.12/0.2 | 13.25±1 | 0.14/0.2 | 13.2±1 | 0.13/0.2 | 13.3±0.95 | 0.17/0.06 |
| Group 2 | 12.8±1.2 | 0.10/0.2 | 12.8±0.97 | 0.10/0.1 | 12.9±0.97 | 0.12/0.2 | 12.85±0.92 | 0.10/0.2 |
| Group 3 | 12.5±1.25 | 0.2/0.09 | 16.1±1.6 | 0.1/0.2 | 17.7±1.53 | 0.14/0.2 | 20.45±4 | 0.17/0.06 |
| ***Prothrombine Time (seconds)*** | | | | | | | | |
| Group 1 | 13.45±1.2 | 0.09/0.2 | 13.5±1 | 0.09/0.2 | 13.6±1.27 | 0.11/0.2 | 13.55±1.17 | 0.11/0.2 |
| Group 2 | 13.1±0.85 | 0.12/0.2 | 13.05±0.7 | 0.17/0.01 | 13.25±1.18 | 0.15/0.13 | 13.4±0.9 | 0.13/0.2 |
| Group 3 | 13.6±1.3 | 0.09/0.2 | 16.1±1.6 | 0.19/0.02 | 18.1±1.8 | 0.14/0.2 | 22.6±1.5 | 0.16/0.09 |

**Group 1:** (control groupe) force-fed throughout the experiment with distilled water ; **Group 2:** Forced fed with Rice; **Groupe 3:** force-fed with a solution of ginseng 5%; **KS**: Komogorov Smironov Test:,***p*:** significance value ; **T0**: the beginning of the forced-feeding ; **T1**: 15days of forced-feeding ; **T2**:30days of forced feeding ; **T3**: 45days of forced-feeding

We found no effect even for prolonged force-feeding with rice flour solution on the median values of prothrombin time, as we did with activated partial thromboplastin time. At T0 and T3, the median values of this variable in the control group were 13.451.20 sec [CI95 %: 13.10-13.86] and 13.551.17 sec [CI95 %: 13.33-13.97], respectively. The median activated partial thromboplastin time for group 2 varied slightly, with median values of 13.451.2 sec [CI95 %: 13.10-13.86] at T0 and 13.551.17 sec [CI95 %: 13.33-13.97] at the end of the experiment. On the other hand, the activated partial thromboplastin time, was prolonged in the ginseng solution group, with median values ranging from 13.61.3 sec [CI95 %: 13.29-13.92] at T0 to 22.61.5 sec [CI95 %: 21.89-23.14] at T3.

The preliminary comparative study at T0 using the Kruskal Wallis (KW) test revealed no significant difference in thrombocyte values (G1vsG2 vs G3: KW=2/$p$=0.72). There is no discernible difference throughout force-feeding. For the other coagulation parameters, the comparative study revealed significant differences in the activated partial thromboplastin time at T2 and T3 with G1vsG2vsG3: KW=2/$p$=0.02 and KW=2.2/$p$=0.013). The prothrombin time values differed significantly across all groups as well.

These differences are more visible with the Mann-Whitney test as a post hoc analysis. During the experiment, a difference is mostly observed between the group that received the ginseng solution and the other groups. It is only from T1 that the rate of group 3 prothrombin time remain is significantly different from group 1 and 2 rate's (U=32/*p*=0.01 at T2 U=33/*p*=0.02 at T3 and T3). At T2 and T3, the prothrombin time values in groups 1 and 3 remain significantly different (Table 2).

Table 2 : Post hoc analysis with Mann Whitney test

| | Thrombocytes | | Prothrombin time (PT) | | Activated Partial thromboplastic time (aPPT) | |
|---|---|---|---|---|---|---|
| | U test | *p* | U Test | *p* | U test | *p* |
| **Group 1 vs Group 2** | | | | | | |
| At T0 | 235 | 0.53 | 217 | 0.14 | 224 | 0.18 |
| AtT1 | 254 | 0.82 | 208 | 0.10 | 213 | 0.124 |
| AtT2 | 215 | 0.28 | 216 | 0.14 | 208 | 0.191 |
| At T3 | 231 | 0.46 | 205 | 0.10 | 206 | 0.19 |
| **Group 1 vs Group 3** | | | | | | |
| AtT0 | 250 | 0.75 | 267 | 0.67 | 229 | 0.226 |
| AtT1 | 228 | 0.42 | 32 | 0.01* | 13.5 | 0.02* |
| AtT2 | 219 | 0.32 | 1.1 | 0.012* | 1.4 | 0.015* |
| AtT3 | 188 | 0.10 | 0.05 | <0.01** | 0.9 | 0.001** |
| **Group2vs Group3** | | | | | | |
| AtT0 | 237 | 0.56 | 186 | 0.36 | 279 | 0.86 |
| AtT1 | 258 | 0.89 | 33 | 0.02* | 8 | 0.01* |
| AtT2 | 240 | 0.59 | 17.5 | 0.011* | 0.2 | 0.01* |
| AtT3 | 173 | 0.10 | 1.5 | <0.01** | 1.5 | 0.01* |

U test : Man Whitney Test ; *p* : Signification level: T0: T1; T2 T3

The same finding for the activated partial thromboplastin time, with significant differences between groups 1 and 3 at T1 (U=13.5/*p*=0.02), T2 (U=1.4/*p*=0.015), and T3 (U=0.9/*p*=0.01) (Table 2). At T1, T2, and T3, the activated partial thromboplastin time values differed between the groups that received rice powder (Group 2) and the Ginseng solution (Group 3).

The comparative analysis shows that the values of thrombocytes in group 3 are remote values at T1, T2, and T3 (Fig. 1), which justified the spacing of points on the curves of the evolution of prothrombin and activated partial thromboplastic time in this same group (Fig. 2 and Fig. 3).

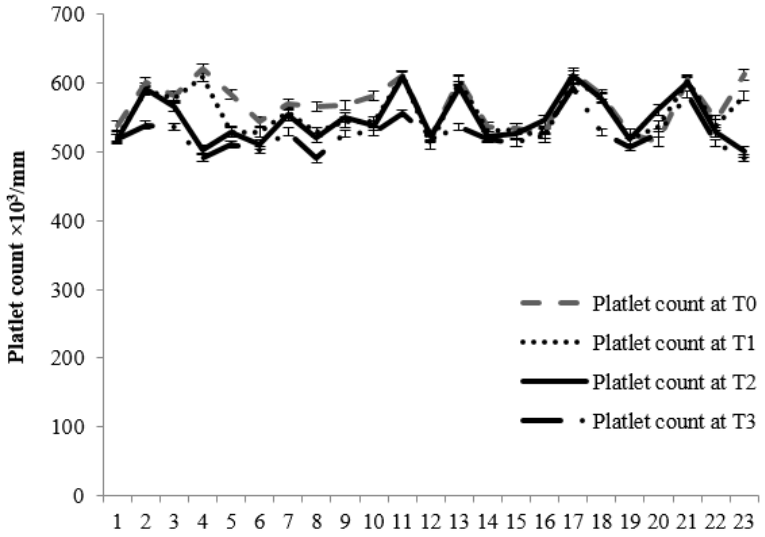


Figure 1: The evolution of plateletcount values in the experimental group

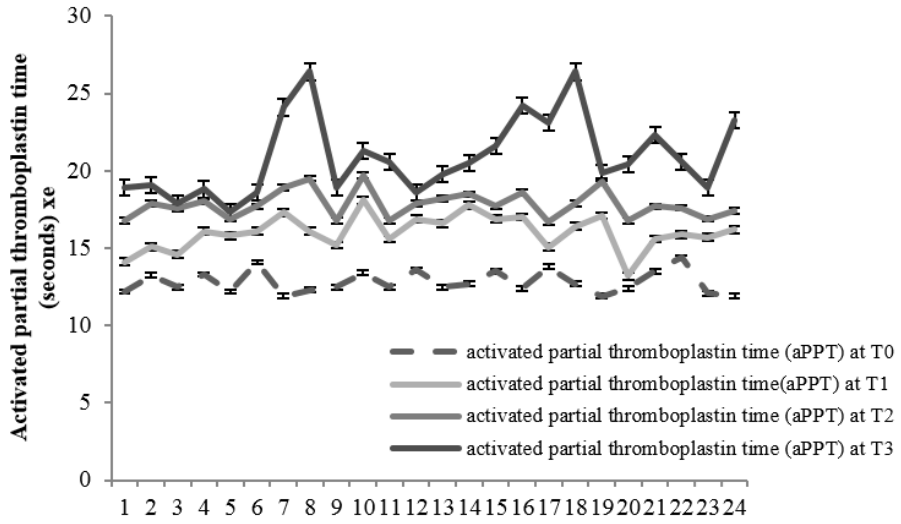


Figure 2: Evolution of Activated partial thromboplastin time (seconds)

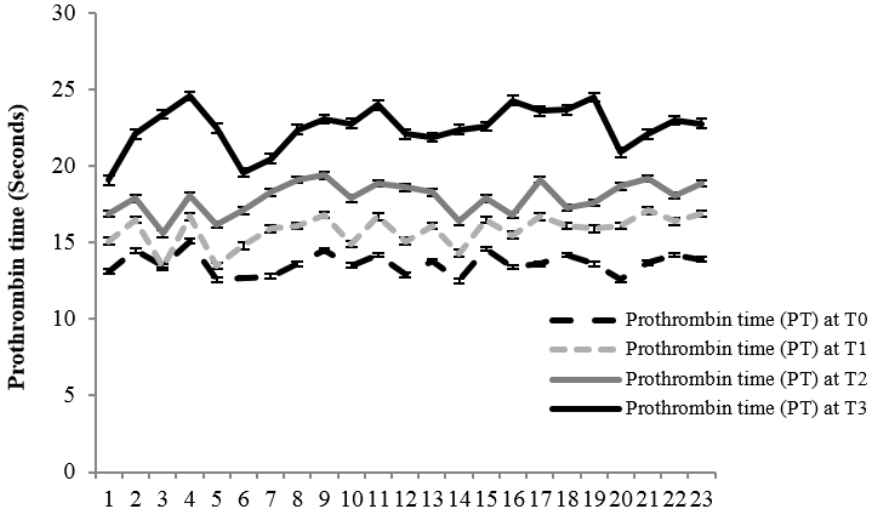


Figure 3: Evolution of prothrombin time in group 3 (Foced fed with *Panax ginseng*) in group 3 (Forced fed with *Panax ginseng*)

The Wilcoxon paired sample test used to investigate the evolution of the variables studied during the experiment. This comparison revealed that thrombocyte levels in the groups did not change significantly throughout gavage, although there was a slight but not significant decrease in the group receiving ginseng from T2 and T3 (Z=-4.167/$p$=0.05) and (Z=4.04/$p$=0.05), respectively (Table 3). The difference is observed significantly for the values of prothrombin time and activated partial thromboplastin time in the Ginseng group. Indeed, a significant prolongation of prothrombin time and partial thromboplastin time, which is observed with T2 for the prothrombin time (Z=-4.2/$p$<0.01) and from T1 for the partial thromboplastin time activated (-4.28 / $p$<0.01) (Table 3).

Table 3: A comparison of coagulation parameters using the Wilcoxon test

| | **Thrombocytes** | | **Prothrombin time (PT)** | | **Activated Partial thromboplastic time (aPPT)** | |
|---|---|---|---|---|---|---|
| | Z (Wilkoxon) | *p* | Z (Wilkoxon) | *p* | Z (Wilkoxon) | *p* |
| **Group 1** | | | | | | |
| T0 vs T1 | -2.58 | 0.29 | -1.88 | 0.21 | -1.13 | 0.22 |
| T1 vs T2 | -2.93 | 0.3 | -0.204 | 0.838 | -1.117 | 0.26 |
| T2 vs T3 | -2.49 | 0.1 | -1.09 | 0.272 | -1.16 | 0.24 |
| T0 vs T2 | -3.65 | 0.1 | -2.54 | 0.19 | -1.52 | 0.128 |
| T0 vs T3 | -4.04 | 0.19 | -2.09 | 0.36 | -1.703 | 0.09 |
| **Group 2** | | | | | | |
| T0 vs T1 | -2.09 | 0.24 | -0.79 | 0.62 | -0.74 | 0.65 |
| T1 vs T2 | -2.43 | 0.15 | -0.46 | 0.646 | -0.16 | 0.87 |
| T2 vs T3 | -1.308 | 0.19 | -0.60 | 0.79 | -0.04 | 0.96 |
| T0 vs T2 | -1.49 | 0.136 | -0.628 | 0.53 | -1.26 | 0.205 |
| T0 vs T3 | -1.12 | 0.26 | -1.43 | 0.152 | -0.61 | 0.54 |
| **Group 3** | | | | | | |
| T0 vs T1 | -3.28 | 0.08 | -4.11 | 0.051 | -4.31 | 0.03** |
| T1 vs T2 | -3.65 | 0.06 | -4.16 | 0.05 | -4.28 | <0.01** |
| T2 vs T3 | -1.55 | 0.12 | -4.2 | <0.01** | -4.29- | <0.01** |
| T0 vs T2 | -4.167 | 0.05 | -4.19 | <0.01** | -4.28 | <0.01** |
| T0 vs T3 | -4.04 | 0.11 | -4.19 | <0.01** | -4.27 | <0.01** |

Throughout force-feeding, this prolongation is observed for both parameters significantly (Table 3). They are clearly represented by ladder curves in ginseng group (Fig. 2 and Fig. 3), in contrast to the almost overlapping thrombocyte values (Fig.1).

## DISCUSSION

The thrombocyte values for all combined groups ranged from $454\times10^3$ / $mm^3$ to $660\times10^3$ / $mm^3$, remaining within the normal minimum and maximum limits recommended for certain rodents by Santos et *al.* [17] of $315\times10^3$ / $mm^3$ to $758\times10^3$ / $mm^3$ for the web star, 285 to $890\times10^3$ / $mm^3$ for C57BL/6 mice, and 325 to 888 $10^3$ / $mm^3$ for Balb/c mice [17]. Although significant variations in coagulation test values may appear due to the animal's age and sex [17, 18, 19 and 20], prothrombin time values fluctuated between 11.9 and 24.6 sec, remaining relatively high compared to the data indicated by Lemini et *al.* [18] with 7.9–14.5 sec for CD1 male mice, but close to the data from the Wistar rat, which indicated prothrombin time values between 13.9–21.1 sec [18]. The same observation is made for of actived partial thromboplastin time, where our data remain close to the Wistar rats' (23.9–43.0 sec) and CD1 mice's (15.5-23.1 sec) [18].

Several authors [5, 6, 7, 21 and 22] were interested in the effect of ginseng biomolecules on blood coagulation parameters. Although ginseng is still widely used in traditional Chinese medicine for cardiovascular disease prevention (coronary heart disease, myocardial infarction, angina pectoris, cerebral ischemia) [23], antioxidant [24, 25], and hepatoprotective effects [26, 27], pharmacological studies on the coagulation mechanism remain controversial [4, 6]. Lau et *al.* [7] reported in 2009 that 500mg/kg of raw and steamed *Panax notoginseng*, *Panax ginseng*, and *Panax quinquefolium* inhibited coagulation factors and increased bleeding time [7]. Clearly, our findings are in line with the observed effects, as we observed a decrease in platelet counts among the *Panax ginseng* solution group, though this was not statistically significant. Other previous studies [28, 29 and 30], reported similar effects of platelet aggregation inhibitors, which were attributed to the saponins found in *Panax ginseng*, which increase the fluidity of platelet membranes and inhibit the collagen responsible for platelet aggregation [7, 31]. Ginsenoside Rk1, Rg1, F4, Rg3-RGE, Rp3, Rp4, and gintonin have antiplatelet activity. Rp1 has also been shown to inhibit granule secretion, mobilize calcium ions, activate integrin IIb3, and increase cAMP levels [11, 32]. Several other studies have found that red ginseng directly inhibits platelet aggregation via the nuclear factor-B and mitogen-activated protein kinase signaling pathways. [33]. However, in the current study, the lack of a significant effect of *Panax ginseng* on the antiplatelet potential could be attributed to composition, in particular the proportions of the fractions of saponins and non-saponins contained in *Panax ginseng*, or to a short duration of administration of ginseng . This reduced the exposure time of thrombocytes to ginseng and reduced the fluidification mechanism of the platelet membranes.

Other authors suggest that antiaggregant effects is attributed to highly variable non-saponin or lipophilic fractions (phenol compounds, acid polysaccharides, and polyethylene, as well as antiplatelet compounds such as guanosine and ginsenoside [34]. While the anticoagulant potential of ginseng has been widely documented, it is worth noting that ginseng is linked to a few cases of spontaneous bleeding, but it is also linked to reports of subtherapeutic INR and thrombosis in patients who were previously stable on warfarin [35, 36]. However, interactions with anticoagulant drugs remain highly controversial, as Chua et *al.* [37], reported in a randomized, open-label, and controlled study that taking ginseng (*Panax ginseng*) had no effect on the pharmacological action of warfarin [37]. Considering that, ginseng's antiplatelet activity is not sytematically linked to thrombocytopenia [38]. We must also considered its pharmacokynetic specificity and half-life [39], particularly the metabolite Rq and its coumpound K [40]. The study of platelet functions seems necessary to better understand the effect and mode of action of ginseng on platelets.

In contrast,our findings indicate a strong and significant prolongation of the prothrombin time following the force-feeding of mice with *Panax ginseng* solution. Yun et *al.* [41] reported the same finding, with the control group having a prothrombin time of 14.7s 0.7 and the group receiving 2mg / mL of Korean red ginseng extract having a prothrombin time of 15.6s 0.0 [41]. Lau et *al.* [7] made the same recommendations with the study of the anticoagulant effects of *Panax notoginseg* [7], despite differences in prothrombin time prolongation isattributed to administered doses. Indeed, a study on the effect of medicinal herbs on platelet function and coagulation, found that crude extracts of *Panax notoginseng* prolonged prothrombin time proportionally to concentration [42].

Prothrombin time PT prolongation is associated with an influence of the extrinsic and common pathway of coagulation [13, 43], with the factors involved in this coagulation pathway being I (Fibrinogen), II (Prothrombin), and V (Proaccelerin) [44]. For fibrinogens, Kim et *al.* [45], found that rats fed ginseng berry extract had higher levels of fibrinogen breakdown products in serum [45]. Ginseng's effect on proaccelerin (FactorV) is explained by the inactivation of prothrombinase complex [46], especially when coupled to the active form of the coagulation factor FX10 [5, 46], which could inhibit the conversion of prothrombin to thrombin. Although the mechanism of inhibition is unknown, Neville [46], reported that the compounds ginsenoside Rg2, Rg3, and protopanaxtriol, PPT are potential natural inhibitors of FXa and may be involved in the proaccelerin inhibition pathway.

Unlike prothrombin time, activated partial thromboplastin aPPT time primarily investigates the intrinsic and common coagulation pathway [16, 47], in which the coagulation factors involved are primarily factor XII, XI, IX, X, VIII, II, and I [48, 49]. Prolongation of activated partial thromboplastin time after ginseng administration is reported, particularly after administration of a high concentration of *Panax ginseng* raw extract (6.7mg/L) [7]. The inhibition of this pathway, could be caused by the inactivation of the conversion of Factor XII (a zymogen, inactivated serine protease) into Factor XIIA (activated serine protease) [50], which could alter the catalysis of Factor IXA into Factor X then into Factor Xa, at the end of the cascade due to the inhibitory action of the triterpenoids found in *Panax ginseng.*

## CONCLUSION

The current study found that *Panax ginseng* has a strong influence on coagulation parameters. In contrast to previous research, our findings suggested that *Panax ginseng* has an anticoagulant rather than an antiplatelet effect. However, this study has some limitations, including a small sample size and the use of a single experimental model, as well as the use of the number of platelets as the only indicator of the anti-aggregating effect of *Panax ginseng.* The study is limited by the use of a single variety of *Panax ginseng*, other varieties of ginseng such as *Panax notoginseng* and *Panax quadfifolium* were desirable to be used in other experimental animal models as a variable dose administration. While the coagulation cascade has been extensively studied, the impact of active compounds on the intrinsic and extrinsic coagulation pathways has not yet been studied. Toxicity and histological studies appear to be required to provide additional elements of a dose-anticoagulant response. Two major conclusions can be drawn from this work : *Panax ginseng* may have potent anticoagulant properties in vitro, although it is important to undertake studies with large sample sizes to characterize the health effects of its interactions.

The antiaggregant effect of *Panax ginseng* should be studied in more detail. Particularly in the study of aggregate functions associated with platelet count.

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