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# INDUCED COAGULATION AS A COMPLICATION OF INFLAMMATORY REACTIONS IN MICE TREATED WITH MONOSODIUM GLUTAMATE

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**ABSTRACT:** Monosodium glutamate (MSG) is a familiar food additive processed to enhance the taste. This work was carried out to investigate the effect of MSG on platelets profile and indices of thrombus formation together with the detection of some plasma inflammatory markers. The study used adult male mice divided into five groups: a control group and four groups treated with different doses of MSG (2, 4, 8 and 16 mg/kg, respectively for 30 days, orally). The mice treated with 8 and 16 mg/kg of MSG resulted in significant high levels of plasma inflammatory markers such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) and C-reactive protein (CRP). Also, thrombocytosis, significant increase in fibrinogen (FIG) concentration, low values of prothrombin time (PT) and the associated international normalized ratio (INR) compared to the control group. Our study suggests that MSG initiates inflammatory reactions, which may induce thrombocytosis and coagulation complication in mice model.

**INTRODUCTION:** Nowadays, monosodium glutamate (MSG) is one of the world's most widely flavor enhancer. When it is added to food in relatively small quantities, the palatability of this food increases [1, 2]. Although, MSG consumption is believed to be safe, The Joint FAO/WHO Expert Committee on Food Additives (JECFA) did not specify the acceptable daily intake for glutamic acid and its salts [3]. The current work targeted the assessment of the risk of oral administration of MSG on coagulation hemostasis along with inflammatory response in mice model.

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Several empirical studies correlate long consumption of MSG with a series of unwanted symptoms. Moreover, it caused some toxic effects and increased the oxidative stress in liver, heart and erythrocytes, kidney and nervous system [1, 4, 5, 6]. Also, the oral ingestion of MSG to rats or mice results in a condition of inflammatory blood vessels, oxidative stress in many tissues, referred to hyperlipidemia, hypolipoproteinemia, and hyperglycemia and causes the condition of atherosclerosis [6, 7, 8, 9]. Thrombocytosis has been associated with the risk of thrombotic and hemorrhagic events.

Findings among patients with mild thrombocytosis suggested that high normal platelet count is associated with the occurrence of thrombotic events [10]. Thrombocytosis may be a reactive process (secondary thrombocytosis), which is a secondary to a variety of acute and chronic clinical conditions

including acute infection or inflammation, response to exercise and acute blood loss [11, 12]. MSG has a significant increase in the number of platelets; thrombocytosis, bleeding time and clotting time in rats [13]. The Effect of MSG showed cessation of bleeding and accelerate the thick fibrin formation at wound tissue of rat-tail. Also, MSG shortens thrombin time and prolongs euglobulin lysis times which signify antifibrinolytic effects; it was reported to stop bleeding and constrict blood vessels by administration locally [14, 15].

## MATERIAL AND METHODS:

**Animals:** The present study use (60) adult male albino mice, weighing (50±5 g). Animals housed in environmentally controlled conditions (temperature of 22±2 ºC) with a 12 h light/dark cycle and had free access to commercial rodent pellets and water *ad libitum*. The Experimental Animal Ethics by the National Institutes of Health Guide for Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1996).

**Experimental Design:** Mice divided into 5 groups (n= 12) as follows: First control group (mice treated with oral distilled water). Second to fifth treated groups (mice treated with oral doses of MSG (2 mg/kg b wt.); MSG (4 mg/kg b wt.); MSG (8 mg/kg b wt.) and MSG (16 mg/kg b wt.), respectively. All treatments for 30 consecutive days.

**Chemicals:** Monosodium glutamate (L-Glutamic acid monosodium salt). Empirical Formula $C_5H_8NNaO_4$. × $H_2O$. The salt of the current study purchased from local markets in Saudi Arabia called Aji-no moto.

**ELISA Cytokines:** Estimation of plasma TNF-α (Cat. no. 88-7324-22), the sensitivity of TNF-α was 8 pg/ml; plasma IL-6 (Cat. no. EM2IL6) were calculated from standard curves, the sensitivity of IL-6 was 7 pg/ml and plasma CRP (Cat. no. EPX01A-26045-901). All the mouse ELISA kits used according to the manufacturer's instructions; Thermo Fisher Scientific Company.

**Platelets Profile:** Platelets counts, MPV, PDW, and PCT profiles obtained, as a part of complete blood count profiles according to the manufacturer's instructions by using automated hematology analyzer (SysmaxKX 21, Germany) is a double capillary instrument. Samples were analyzed.

**Coagulation Profile:** 200 µl of blood was collected into a citrated (blue-top) tube containing (3.2% sodium citrate) to measure PT and INR by using a coagulation analyzer through the conventional procedures used for human blood coagulation analysis [16]. Quantitative estimation of plasma fibrinogen antigen by total ELISA kit Catalog no. IMFBGNKT, Innovate Research Company.

**Statistical Analysis:** Reported values represent mean ± SE. The statistical analysis evaluated by one-way ANOVA. Once a significant F test obtained, LSD comparisons performed to assess the significance of differences among various treatment groups. Statistical Processor System Support "SPSS" for Windows software, Release 21.0 (SPSS, Chicago, IL) was used.

**RESULTS AND DISCUSSION:** Recently, several empirical studies reported that inflammation and coagulation complications are intricately linked, which significantly associated with morbidity and mortality. The current new approach may be a link between the MSG-induced inflammatory response and the development of coagulation complications in mice models.

**TABLE 1: EFFECT OF MSG TREATMENTS ON PRO-INFLAMMATORY CYTOKINES**

| Groups / Parameter | Control | 2 MSG | 4 MSG | 8 MSG | 16 MSG |
|---|---|---|---|---|---|
| TNF-alpha (Pg/ml) | 245.0 ± 0.62 | 287.00 ± 0.86$^{*}$ | 309.42 ± 0.79$^{*a}$ | 440.38 ± 2.84$^{*ab}$ | 631.93 ± 2.60$^{*abc}$ |
| CRP (Pg/ml) | 2.07 ± 0.00 | 2.09 ± 0.01$^{*}$ | 3.01 ± 0.04$^{*a}$ | 5.41 ± 0.03$^{*ab}$ | 8.36 ± 0.03$^{*abc}$ |
| IL-6 (Pg/ml) | 412.92 ± 1.39 | 414.94 ± 0.68$^{*}$ | 563.59 ± 0.99$^{*a}$ | 656.35 ± 7.02$^{*ab}$ | 944.33 ± 5.02$^{*abc}$ |

Data expressed as Mean ± SE. (n=12). One Way analysis performed between groups with LSD post hoc test with significance level 0.05. Significant indicated by an asterisk (*) as compared to control, (a) as compared to 2 MSG group, (b) as compared to 4 MSG group, (c) as compared 8 MSG group

Data in **Table 1** presented a significant increase in the proinflammatory cytokines (CRP and TNF) as well as interleukin-6 (IL-6) in all treated groups as compared to control group. 8 and 16 MSG results showed a significant increase in the pro-inflammatory cytokines values as compared to all

groups corresponding values. Results of 16 MSG group recorded a significant increase in the measured cytokines and interleukin-6 values as compared to the corresponding values 8 MSG group. As well as 4 MSG showed a significant increase in data as compared to 2 MSG value.

A significant increase in plasma TNF, IL-6, and CRP in mice treated with 8 and 16 mg/kg of MSG confirming the inflammatory effects of MSG which in line with previous studies [8, 9]. On the other hand, 2 and 4 mg/kg doses didn't affect significantly these cytokines. As the increasing level of plasma TNF-α, is the best pro-inflammatory cytokine released at the site of inflammation, also, TNF-α promotes a procoagulant state by inhibiting synthesis of the anticoagulant protein and stimulating thrombin and fibrin formation. IL-6 has linked to the activation of coagulation in mice model. Also, a high level of plasma IL-6 increase the transcription of procoagulant proteins or decrease the transcription of anticoagulant proteins. CRP; the transcriptional target of IL-6 is linked to ischemic cardiovascular complications [17, 18, 19]. Inflammation stimulates the unbalance between pro and anticoagulant properties of endothelium, increases the fiber density and resists the fibrinolysis in patients with acute coronary syndromes [20].

During inflammation, platelets release micro-particles containing tissue factor for a localized induction of the coagulation cascade [21]. Several animal studies revealed those inflammatory diseases such as inflammatory bowel disease (IBD) associated with elevated TNF-α, IL-6 and IL-1beta; the pro-inflammatory cytokines that enhanced thrombus development [22].

**TABLE 2: EFFECT OF MSG TREATMENTS ON PLATELETS PROFILE**

| Groups / Parameter | Control | 2MSG | 4 MSG | 8 MSG | 16 MSG |
|---|---|---|---|---|---|
| Platelets count 103/µL | 508.40 ± 3.25 | 512.20 ± 3.86 | 518.50 ± 6.51 | 1139.00 ± 11.12 *ab | 1623.40 ± 9.31 * abc |
| MPV (fl) | 6.56 ± 0.02 | 6.66 ± 0.04 | 6.59 ±0.06 | 7.76 ± 0.05 *ab | 7.72 ± 0.14 *ab |
| PDW (fl) | 8.14 ± 0.03 | 8.21 ± 0.01 | 8.21 ± 0.03 | 8.30 ± 0.03 *ab | 8.40 ± 0.03 *abc |
| PCT % | 6.55 ± 0.02 | 6.54 ± 0.02 | 6.52 ± 0.04 | 13.1 ± 0.16 *ab | 16.6 ± 0.07 *abc |

Data expressed as Mean ± SE. (n=12). One Way analysis performed between groups with LSD post hoc test with significance level 0.05. Significant indicated by an asterisk (*) as compared to control, (a) as compared to 2 MSG group, (b) as compared to 4 MSG group, (c) as compared 8 MSG group.

Platelets profiles have a central role in the process of inflammation; they are correlated with the activation of the coagulation system during inflammatory reactions and thrombotic diseases [23]. Data in **Table 2** showed a significant increase in platelets count, MPV, PDW and PCT% in groups treated with MSG at doses 8 and 16 mg/kg b. wt for 30 consecutive days as compared to control values and other treated groups. The data showed a significant increase in platelets count, PDW and PCT% in 16 MSG group as compared to 8 MSG group while recorded not statistically differences in MPV. Meanwhile, mice were treated with 2, and 4 mg/kg showed healthy compared to the control group in all the previous parameters. These data agree with Ajibola *et al*., [13] platelets, MPV, PDW, and PCT have been shown to have diagnostic value in certain inflammatory diseases, such as inflammatory bowel diseases, atherosclerosis [24, 25]. On the other hand, Lin *et al*. reported that MPV is a predictive indicator in patients with portal vein thrombosis [26]. The present data in mice treated with oral 8 and 16 mg/kg showed the type of thrombocytosis that is in agreement with previous studies of secondary thrombocytosis in the setting of systemic disorders due to inflammation or acute blood [27, 28, 29].

Moreover, thrombocytosis may be related to increasing levels of circulating cytokines, in particular, interleukin IL 6; the proinflammatory cytokine is known to regulate promote megakaryocytopoiesis *in-vitro* and raises platelet counts *in-vivo* [30]. In hemostasis, platelet production is tightly regulated by the hormone thrombopoietin (TPO), which regulates nearly all stages of the megakaryocytopoiesis and this explains that alteration in megakaryocytes and platelets production leading to thrombocytopenia or thrombocytosis [31, 32]. Increasing the level of interleukin-6 induce the expression of TPO in hepatocytes. TPO mainly regulates the homeostatic production of platelets and the TPO receptor (MPL)/JAK2 axis [33. 32]. The present data agreed with Chu *et al*., [34] who reported that MPV is associated with high-grade inflammation owing to

the presence of the large platelets in circulation. In addition, MPV is found to be associated with cytokines (thrombopoietin, interleukin-6, and interleukin-3) that regulate the production of larger platelets and promote megakaryocyte production [19]. Our results showed a significant increase in PDW and PCT in groups 8 and 16 mg/kg compared to control group; the results are in line with the previous reports, which resulted that MPV and PDW usually affected in the same direction [35]. On the other hand, conflicting results showed there is no direct relationship between MPV and PDW [36, 37]. The current results demonstrated a high percentage of PCT; the volume occupied by platelets in the blood.

**TABLE 3: EFFECT OF MSG TREATMENTS ON COAGULATION PROFILE**

| Groups / Parameter | Control | 2MSG | 4 MSG | 8MSG | 16 MSG |
|---|---|---|---|---|---|
| Fibrinogen (ng/ml) | 250.38 ± 0.03 | 264.04 ± 1.9* | 266.48 ± 1.63* | 351.17 ± 3.54*ab | 523.59 ± 4.80*abc |
| PT (sec) | 8.31 ± 0.04 | 8.28 ± 0.07 | 8.38 ± 0.13 | 5.36 ± 0.16*ab | 3.25 ± 0.45*abc |
| INR | 0.91 ± 0.00 | 0.92 ± 0.00 | 0.91 ± 0.01 | 0.69 ± 0.01*ab | 0.38 ± 0.02*abc |

Data expressed as Mean ± SE. (n=12). One Way analysis performed between groups with LSD post hoc test with significance level 0.05. Significant indicated by an asterisk (*) as compared to control, (a) as compared to 2 MSG group, (b) as compared to 4 MSG group, (c) as compared 8 MSG group.

The marker for the extrinsic coagulation pathway measured by calculating the prothrombin ratio along with the international normalized ratio. Data in **Table 3** showed a significant increase in fibrinogen concentration in all treated groups as compared to control value. While revealed a significant decrease in PT and associated INR in 16 MSG group as well as 8 MSG group as compared to control and all other treated groups. The results of our study showed the onset of thrombosis in mice treated with 8 or 16 mg/kg MSG through significant elevating in fibrinogen concentration and the decrease the PT and associated INR. Fibrinogen (factor I) is an acute-phase protein that it may be elevated during tissue and vascular inflammation. Fibrinogen is the substrate of thrombin which converted it to fibrin in the coagulation cascade provides the fibrin-based blood clot [38, 39]. Elevation fibrinogen concentration discussed previously as fibrinogen released from mega-karyocytes and linked to inflammation [40]. Also, elevated plasma fibrinogen is indicator factor for thromboembolism or atherosclerosis [41].

**CONCLUSION:** The risk for thrombus formation at high doses of MSG (8 and 16 mg/kg) in mice model may be correlated with inflammation, thus it needs more research to be done to be fully investigated.

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## REFERENCES:

1. Rosa SG, Chagas PM, Pesarico AP and Nogueira CW: Monosodium glutamate-induced nociception and oxidative stress-dependent on the time of administration, the age of rats and susceptibility of spinal cord and brain regions. Toxicol Appl Pharmacol 2018; 35: 64-73.
2. Zanfirescu A, Cristea AN, Nitulescu GM, Velescu BS and Gradinaru D: Chronic monosodium glutamate administration induced hyperalgesia in mice. Nutrients 2017; 10: 1.
3. Ly HQ, Kirtane AJ, Murphy SA, Buros J, Cannon CP, Braunwald E and Gibson CM: Association of platelet counts on presentation and clinical outcomes in ST-elevation myocardial infarction (from the TIMI Trials). Am J Cardiol 2006; 98: 1-5.
4. Vindini NA, Nayantara AK, Ramaswamy C, Gowda D, Ahmed B and Bhat R: Study on the evaluation of monosodium glutamate-induced oxidative damage on renal tissue on adult Wistar rats. J Chin Clin Med 2010; 3: 112-115.
5. Pavlovic V and Sarac M: The role of ascorbic acid and monosodium glutamate in thymocyte apoptosis. Bratisl Lek Listy 2010; 111: 357-360.
6. Quines CB, Rosa SG, Chagas PM, da Rocha JT, Dobrachinski F, Carvalho NR, Soares FA, da Luz SC and Nogueira CW: Homeostatic effect of p-chloro-diphenyl diselenide on glucose metabolism and mitochondrial function alterations induced by monosodium glutamate administration to rats. Amino Acids 2016; 48: 137-148.
7. Boonnate P, Waraasawapati S, Hipkaeo W, Pethlert S, Sharma A, Selmi C, Prasongwattana V and Cha'on U: Monosodium glutamate dietary consumption decreases pancreatic $\beta$-cell mass in adult Wistar rats. PLoS One 2015; 10: e0131595.
8. Wang WF, Li SM, Ren GP, Zheng W, Lu YJ, Yu YH, Xu WJ, Li TH, Zhou LH, Liu Y and Li DS: Recombinant murine fibroblast growth factor 21 ameliorates obesity-related inflammation in monosodium glutamate-induced obesity rats. Endocrine. 2015; 49: 119-129.
9. Fortis-Barrera A, García-Macedo R, Almanza-Perez J, Blancas-Flores G, Zamilpa-Alvarez A, Flores-Sáenz J, Cruz M, Roman-Ramos R and Alarcón-Aguilar F: *C. ficifolia* (Cucurbitaceae) modulates inflammatory cytokines and IFN-γ in obese mice. Can J Physiol Pharmacol 2017; 95: 170-177

10. Pedersen OH, Larsen ML, Grove EL, van Kooten Niekerk PB, Bønløkke S, Nissen PH, Kristensen SD and Hvas AM: Platelet characteristics in patients with essential thrombocytosis. Cytometry B Clin Cytom 2018. doi: 10.1002/cyto.b.21642.
11. Wagner DD and Burger PC: Platelets in inflammation and thrombosis arterioscler. Thromb Vasc Biol 2003; 23: 2131-2137.
12. Khaleel KJ, Ahmed AA, Alwash MM and Yasin NY: Mean platelet volume, platelet distribution width and plateletcrit values in differentiating clonal from secondary thrombocytosis. Med J Babylon. 2013; 10: 473-478.
13. Ajibola M: The effects of orally administered monosodium glutamate (MSG) on blood thrombocyte, blood coagulation and bleeding in rats. IOSR J Pharm Biol Sci 2012; 4: 4-8.
14. Vermylen J, Badenhorst PN, Deckmyn H and Arnout J: Normal mechanisms of platelet function. Clin Hemato 1983; 12: 107-51.
15. Thakkum U, Prasanpun S and Tungtrakanpoung R: Effect of monosodium glutamate (MSG) on blood clotting in adult male rats (*R. norwegians*). NU Sci J 2008; 5: 85- 91.
16. Unruh M, Grunow A and Gottstein C: Systemic coagulation parameters in mice after treatment with vascular targeting agents. Thromb J 2005; 3: 21.
17. Yeh ET: CRP as a mediator of disease. Circulation 2004; 109: 11-14.
18. Mutlu GM, Green D, Bellmeyer A, Baker C M, Burgess Z, Rajamannan N, Christman JW, Foiles N, Kamp DW, Ghio A J, Chandel NS, Dean DA, Sznajder JI and Budinger GRS: Ambient particulate matter accelerates coagulation *via* an IL-6–dependent pathway. J Clin Invest 2007; 117: 2952-2961.
19. Gao H, Zhang Q, Chen J, Cooper DKC, Hara H, Chen P, Wei L, Zhao Y, Xu J, Li Z, Cai Z, Luan S and Mou L: Porcine IL-6, IL-1β, and TNF-α regulate the expression of pro-inflammatory-related genes and tissue factor in human umbilical vein endothelial cells. Xenotransplantation 2018; 22: e12408.
20. Undas A, Szuldrzynski K, Stepien E, Zalewski J, Godlewski J, Tracz W, Pasowicz M and Zmudka K: Reduced clot permeability and susceptibility to lysis in patients with acute coronary syndrome: effects of inflammation and oxidative stress. Atherosclerosis 2007; 196: 551-558.
21. Engelmann B, Luther T and Müller I: Intravascular tissue factor pathway-A model for rapid initiation of coagulation within the blood vessel. Thromb Haemost 2003; 89: 3-8
22. Senchenkova E, Seifert H and Granger DN: Hyper-coagulability and platelet abnormalities in inflammatory bowel disease. Semin Thromb Hemost 2015; 41: 582-589.
23. Thachil J: Platelets in inflammatory disorders: a pathophysiological and clinical perspective. Semin Thromb Hemost 2015; 41: 572-81.
24. Öztürk ZA, Dag MS, Kuyumcu ME, Cam H; Yesil Y, Yilmaz N, Aydini M, Kadayifci A and Kepekci Y: Could platelet indices be new biomarkers for inflammatory bowel diseases? Eur Rev Med Pharmaco Sci 2013; 17: 334-341.
25. Ren ZJ, Ren PW, Yang B, Liao J, Liu SZ, Lu DL, Wei X, Liu LR and Dong Q: Mean platelet volume, platelet distribution width and platelet count in erectile dysfunction: A systematic review and meta-analysis. Andrologia 2017; 49. doi: 10.1111/and.12777
26. Lin WY, Lu X, Fan FJ and Hu Y: Predictive effect of mean platelet volume in patients with portal vein thrombosis: Ameta-analysis of case-control studies. Curr Med Sci 2018; 38: 575-581.
27. HO KM, YIP CB and DUFFO: Reactive thrombocytosis and risk of subsequent venous thromboembolism: a cohort study. J of Thromb and Haemost 2012; 10: 1768-1774.
28. Woolcock AD, Keenan A, Cheung C, Christian JA and Moore GE: Thrombocytosis in 715 dogs (2011-2015). J Vet Intern Med 2017; 31: 1691-1699.
29. Deppermann C and Kubes P: Start a fire, kill the bug: The role of platelets in inflammation and infection. Innate Immun 2018; 26: 1753425918789255.
30. Saito H, Kono Y, Murakami Y, Shishido Y, Kuroda H, Matsunaga T, Fukumoto Y, Osaki T, Ashida K and Fujiwara Y: Prognostic significance of platelet-based inflammatory indicators in patients with gastric cancer. World J Surg 2018; 42: 2542-2550.
31. Lambert MP: Platelets in liver and renal disease. Hematology ASH Educ Program 2016; 1: 251-255.
32. Plo I, Bellanné-Chantelot C, Mosca M, Mazzi S, Marty C and Vainchenker W: Genetic Alterations of the thrombopoietin / MPL/ JAK2 axis impacting mega-karyopoiesis. Front Endocrinol (Lausanne) 2017; 12: 234.
33. Schulz C and Massberg S: Platelets in atherosclerosis and thrombosis. Handb Exp Pharmacol 2012; 210: 111-33.
34. Chu SG, Becker RC, Berger PB, Bhatt DL, Eikelboom JW, Konkle B, Mohler ER, Reilly MP and Berger JS: Mean platelet volume as a predictor of cardiovascular risk: A systematic review and meta-analysis. J Thromb Haemost 2010; 8: 148-156.
35. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F and Labrianou I: Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia 2010; 14: 28-32.
36. Mariani E, Filardo G, Canella V, Berlingeri A, Bielli A, Cattini L, Landini M P, Kon E, Marcacci M and Facchini A: Platelet-rich plasma affects bacterial growth *in-vitro*. Cytotherapy 2014; 16: 1294-1304.
37. Chandrashekar V: Plateletcrit as a screening tool for the detection of quantitative platelet disorders. J Hematol 2013; 2: 22-26.
38. Bartlett JW, Stavola BL and Meade TW: Assessing the contribution of fibrinogen in predicting the risk of death in men with the peripheral arterial disease. J Thromb Haemost 2009; 7: 270-276.
39. Ariëns RA: Fibrin (ogen) and thrombotic disease. J Thromb Haemostasis 2013; 11: 294 -305.
40. Göbel K, Eichler S, Wiendl H, Chavakis T, Kleinschnitz C and Meuth SG: The coagulation factors fibrinogen, thrombin, and factor XII in the inflammatory disorders-a systematic review. FrontImmunol 2018; 9: 1731.
41. Azdaki N, Zardast M, Anani-Sarab G, Abdorrazaghnaejad H, Ghasemian MR and Saburi A: Comparison between homocysteine, fibrinogen, PT, PTT, INR and CRP in Male Smokers with/without addiction to opium. Addict Health 2017; 9: 17-23.


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