Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
NLM (National Library of Medicine): ID: (101671502)
Index Copernicus Value 2020: 76.36
Volume 11, Issue 3, May-June: 2022, 01-06

ISSN (Online): 2279-0594
ISSN (Print): 2589-8752

Original Research Article

Excessive Consumption of Garlic as a Nutraceutical may Lead to Transient Coagulopathy-First report

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Article Info: Received 15 March 2022; Accepted 19 May. 2022
DOI: https://doi.org/10.32553/jbpr.v11i3.911
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Conflict of interest statement: No conflict of interest

Abstract:
Garlic is a commonly used spice with multiple health benefits. There are numerous active ingredients in garlic, like organosulphur compounds, saponins, phenolic compounds, and polysaccharides, which can affect the various pathways in the human body through different mechanisms. The positive effects of garlic like preventing hypertension, maintaining a healthy lipid profile, decreasing body fat and many others are well known. This one-dimensional knowledge has led people to consume garlic excessively as a nutraceutical. It is imperative to spread awareness about the potential derangements that unregulated consumption of garlic can exert on the human body so that people can strike a perfect balance and understand the safe limits for garlic consumption. We are presenting first report of a peculiar case of coagulopathy induced due to excessive dietary consumption of garlic. The features of this coagulopathy were its mild severity, asymptomatic presentation, and reversibility after cessation of garlic intake. This abnormality probably occurred due to various interactions at the molecular level between the clotting factors and the bioactive compounds in garlic. As such, intake of garlic may require supervision in patients with an elevated risk of bleeding.
Keywords: Garlic, Nutraceutical, coagulopathy, Clotting factors.

Introduction

Over the years, scientific evidences have demonstrated that the benefits of garlic are way more than just being a flavoring agent. The favorable effects of garlic on lipid profile and blood pressure have proven their role in maintaining a healthy cardiovascular status [1,2]. In addition, the spectrum of the beneficial effects of garlic encompasses its antimicrobial, anti-inflammatory, anti-diabetic, anti-obesity, anti-neoplastic, and antioxidant roles [3]. Garlic produces these effects by virtue of its bioactive ingredients, including organosulfur compounds (like diallyl thiosulfonate (allicin), diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), E/Z-ajoene, S-allyl-cysteine (SAC), and S-allyl-cysteine sulfoxide (alliin)

[4,5,6], saponins (desgalactotigonin-rhamnose, voghieroside D1, sativoside B1-rhamnose, and sativoside R1) [7], phenolic compounds, and polysaccharides (β-resorcylic acid and fructose as their significant components, respectively) [8].

The multitude of health effects of garlic has advocated their use as a nutraceutical but has come with a downside of people consuming garlic in an unregulated manner. It is imperative to know how the excessive consumption of garlic, with its numerous biologically active and interactive compounds, can influence various physiological parameters. This knowledge will act as a caution to people consuming garlic irrationally and assist them in recognizing the potential harms associated with excessive garlic consumption. We present first report of a peculiar case of asymptomatic coagulopathy induced by excessive garlic intake. Evidence regarding the effects of garlic on the coagulation profile is scarce, and most studies are animal-based. This case study describes the nature and extent of garlic-induced coagulopathy and discusses the mechanisms likely responsible for it.

Material and Methods

Case Presentation

The primary care physician referred a 35-year-old patient to our hematology and oncology clinic when her routine blood tests depicted an abnormal coagulation profile with prolonged PT and INR values of 18.5 and 1.76, respectively. Her PTT values were normal at 32.4. The patient had no active complaints, or symptoms and her lab reports, including platelet counts, WBC counts and electrolyte levels were within the normal limits. A general workup for coagulopathy including fibrinogen levels, D dimer levels, factor assays, liver function tests, vitamin K levels and antiphospholipid antibodies levels did not reveal any abnormal findings. The patient denied any family history of coagulopathy. Medication reconciliation was performed, which showed no current or past use of any anticoagulants, antiplatelets and antibiotics. As such, there was no direct explanation of her abnormal coagulation profile.

The detailed nutritional history of the patient revealed that she consumed garlic in excessive amounts. The patient used to consume garlic considering its various health benefits, especially its role in keeping her blood pressure in check. The patient used to mince one clove of garlic and swallow it with water every day (twice one when she got up in the morning and another just before bed). She also used to crush and mix one bulb of garlic in 1 gallon of water, which she drank over the whole day. Furthermore, she used to add garlic in every meal of the day she cooked (2 meals per day) in the form of 2 fresh garlic cloves. In addition, she used to prepare a batch of seasoning using a crushed bulb of garlic and one tablespoon of garlic powder, which she added to flavor her meals regularly. A single batch of seasoning lasted for about ten days. The cumulative addition of all these consumptions quantified her daily garlic intake to approximately 20 grams. This amount turned out to be nearly five times of the recommended daily garlic intake of 4 grams [9]. The patient claimed that she had been consuming this amount of garlic for nearly three months before she made her visit to our office.

Results

Ruling out the other common causes, we hypothesized that excessive garlic consumption might be the reason for her abnormal coagulation profile. Since the patient just had mild coagulopathy without any symptoms, we did not perform any active intervention and decided to monitor the patient after counseling her to stop the consumption of garlic. In the next follow-up visit after six weeks, we ordered the lab tests for the patient measuring her coagulation parameters. The patient's INR and PT levels dropped to 1.2 and 13.1, respectively, demonstrating a 31.81% and 29.18 % decline from the initial values (Table 1). The new aPTT level turned out to be 30, indicating a decline of 8.00%.

Table 1.Coagulation parameters before and after cessation of garlic consumption

Parameter	Initial values	Values after 6 weeks of garlic cessation	Percentage change	Reference values
PT	18.5	13.1	29.18% drop	10.5-13.7
aPTT	32.4	30	8.00% drop	21.5-36.4
INR	1.76	1.2	31.81% drop	0.8-1.2

Discussion

Garlic is a commonly used spice worldwide with numerous beneficial effects, especially on the cardiovascular system. However, the excessive consumption of garlic as a nutraceutical comes with its demerits, as evinced by this case study. The effects of garlic on the coagulation system are not studied widely in humans. This case report describes a patient presenting with mild asymptomatic coagulopathy due to excessive garlic intake and its reversal after dietary cessation. Various active ingredients in garlic are most likely responsible for these clotting abnormalities.

Nature of coagulopathy due to garlic

The coagulopathy seen in the patient due to excessive garlic intake was mild without any active symptoms. The main parameters affected were PT and the INR, suggesting that excessive garlic consumption predominantly affects the extrinsic coagulation system. This finding was further highlighted by the significant drop noted in these parameters after the cessation of garlic intake by the patient. As far as the intrinsic pathway is concerned, there was a slight reduction in the aPTT from the initial high-normal values after discontinuation of the garlic in our case, although it was not significant. These findings suggest that the intrinsic pathway is probably more resilient to the anti-thrombotic effects of garlic. Finally, the rapid improvement in the patient's coagulation profile after dietary restrictions demonstrates the reversible nature of garlic-induced coagulopathy.

Possible mechanisms of garlic induced coagulopathy

The allicin (an organosulfur compound, a major garlic constituent) is known to affect the hemostasis by its inhibitory effect on the platelet aggregation and enhancement of the fibrinolytic system [10]. As a major garlic component with numerous properties, allicin probably affects the coagulation system as well. In rat models, garlic was found to decrease the formation of thrombin and fibrin [11]. Thus, the coagulation system could be inhibited by the reduced secretion or deactivation of the various clotting factors involved in the coagulation cascade. The latter mechanism seems more likely as different organosulfur and phenolic compounds in the garlic possibly inhibit various clotting factors by forming hydrogen bonds with the serine proteases (the basic enzymatic structure of most clotting factors). These hydrogen bonds then prevent activation of these zymogens (clotting factors) by blocking them. The reversible nature of coagulopathy can be explained by the steady decline in the organosulphur and phenolic compounds in the body after cessation of garlic intake, leading to freeing up of spaces in the clotting factors for the enzymatic activation.

The increased vulnerability of the extrinsic pathway to the anti-thrombotic effects of garlic can be attributed to the structural composition of garlic. Garlic, belonging to the Liliaceae family, is rich in steroidal saponins. Some of the steroidal saponins, like the D39 saponins, inhibit tissue factor expression by modulating the PI3K/Akt/GSK3β and NF-κB signaling pathways via the deactivation of non-muscular heavy chain IIA [12]. The tissue factors regulate the extrinsic coagulation pathway via factor (F)VIIa activation, thus explaining the predominant effect on the PT time and the INR values due to garlic. **Figure 1** depicts the possible mechanisms of garlic-induced coagulopathy.

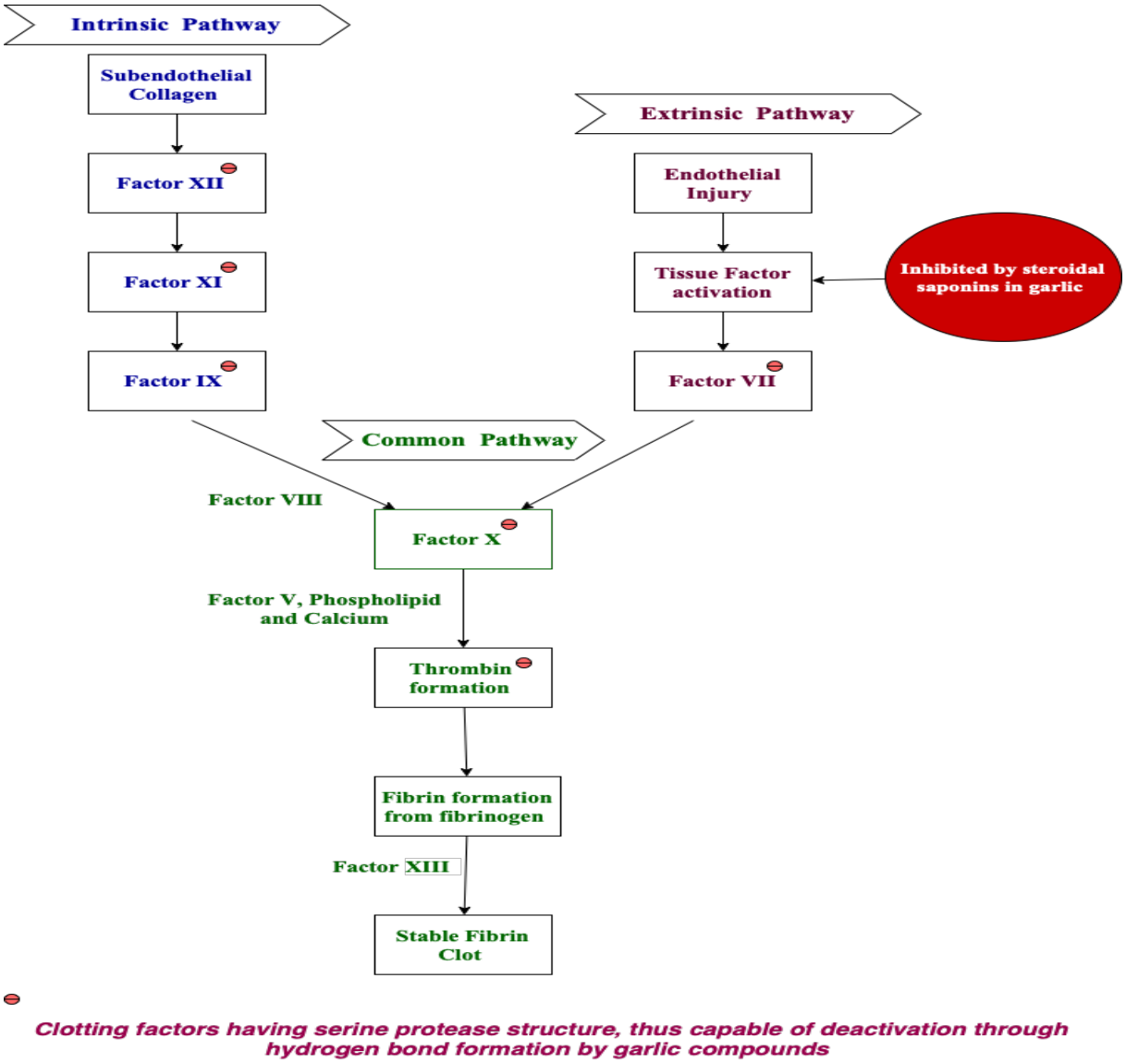

Figure 1: Possible mechanisms of garlic induced coagulopathy Implications of the garlic effects on the coagulation system

Due to the numerous health benefits, garlic consumption as a nutraceutical has increased rapidly. This case study stresses the potential harms of consuming garlic excessively in an uncontrolled fashion. There are multiple ways garlic and its constituents inhibit the clotting process in the blood. Apart from suppressing the platelet aggregation and enhancing the fibrinolytic system, garlic consumed in excess amounts also inhibits the coagulation cascade. Masses across the globe need to be made aware of the elevated bleeding risk with uncontrolled garlic intake. This risk is undoubtedly more detrimental to specific populations than the others. Patients with known hereditary and acquired coagulopathies like hemophiliacs, von Willebrand disease, liver cirrhosis, people on a prolonged course of antibiotics, and anticoagulant medicines need to be seriously counseled about their garlic consumption in a supervised setting. Patients on warfarin should have a regulated and consistent garlic intake in their daily diet as they have to do with vitamin K-rich sources like green leafy vegetables. Women in the reproductive age group should be educated about increased chances of heavy

menstrual bleeds with excessive garlic consumption. Nutritional history quantifying garlic intake is vital in patients presenting with coagulopathy of unknown origin. Furthermore, it is necessary to monitor the garlic intake in patients scheduled for major surgeries to reduce the bleeding risk, as shown in a study by Woodbury et al. [13].

Since the findings of this study are drawn from an isolated case, a limitation of this study is, it cannot provide absolute quantification or set the limits for safe levels of daily garlic intake. More extensive studies comparing the coagulation profiles of subjects consuming different amounts of garlic are needed to reach a consensus on the safety limits. At present, there are no clear guidelines regarding the same.

Conclusion

The role of garlic as a nutraceutical, coupled with its over-the-counter availability, has led to excessive consumption of garlic worldwide. Owing to the chemical interactions between its various bioactive constituents and the clotting factors, garlic can hamper the coagulation cascade in the body when used excessively. Although, the coagulopathy induced by garlic did not produce any active symptoms in this case, this finding certainly calls for making some critical considerations, especially in high-risk patients. Patients with an elevated risk of bleeding due to congenital or acquired causes like hemophiliacs, von-Willebrand deficiency, liver cirrhosis, anticoagulant or antiplatelet use, and patients due for major surgeries should receive adequate supervision regarding their daily garlic intake. The results of the study call for clearcut guidelines from use of nutraceuticals and a strict monitoring of advertisements pertaining to use of nutraceuticals to avoid such adverse events in ignorant public. This also calls for our National and International health care regulatory bodies like World Health Organization (WHO), Uppasala Monitoring Center, Food and Drug Adminstartion to set up some unambiguous advisories on unregulated use/sale/availability of nutraceuticals.

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