Blood Disorders & Transfusion

Reis et al., J Blood Disord Transfus 2016, 7:5
DOI: 10.4172/2155-9864.1000367

Review Article OMICS International

Possible Haematological Abnormalities Induced by Herbal Tea Consumption: A Review

Rengin Reis[1], **Hande Sipahi**[2*] **and Ahmet Aydin**[2]

[1]*Department of Pharmaceutical Toxicology, Karadeniz Technical University, Faculty of Pharmacy, Trabzon, Turkey*

[2]*Department of Pharmaceutical Toxicology, Yeditepe University, Faculty of Pharmacy, İstanbul, Turkey*

[*]**Corresponding author:** Hande Sipahi, Department of Pharmaceutical Toxicology, Yeditepe University Faculty of Pharmacy, İstanbul-34755, Turkey, Tel: +90 216 5780000 (3371); Fax: +90 216 570068; E-mail: hande.sipahi@yeditepe.edu.tr, handesipahi@hotmail.com

Received date: Jul 29, 2016, **Accepted date:** Sep 20, 2016, **Publication date:** Sep 23, 2016

Abstract

Nowadays, a vast majority of herbal products used in traditional medicine are consumed in the form of tea due to their aromas, favourable tastes, and health-boosting effects arising from the antioxidant activity of the phenolic content. Even though people are advised to include these herbal teas in their daily diet as health promoters, the articles in the literature often present conflicting findings on the relationship between herbal tea consumption and haematological parameters. In this review, we recompiled the limited research on the possible relationship between herbal tea consumption and haematological alterations. We suggest that the contributions of active ingredients in the herbal tea products may affect haematological parameters such as the degree of iron absorption, serum ferritin concentration, thrombocyte level, aggregation rate, and lymphocyte mediated immunity. Populations, especially pregnant women and patients under the risk of haematological diseases, should consume these products under the control of physicians or other healthcare professionals. Furthermore, online marketing of these products or via TV commercials should be restricted due to the increasing misusage and related haematological alterations.

Keywords: Herbal products; Herbal extracts; Iron absorption; Thrombocytopenia; Immune system; Haematological parameters

Introduction

Over the last decade, the use of natural remedies such as herbal teas, nutritional supplements, and alternative medicines has increased significantly in many countries owing to the common belief which claims these products are safe to use [1]. According to Vidovic et al. [2], tea production in Serbia has been increased at the rate of 10% annually and so its export to the markets of EU and North America has increased. In Europe, market trends on complementary medicine have been turning to different alternatives based on herbs and aromatic plants with more variety of tastes or with medicinal properties and this approach leads to the proliferation of "Tea shops" and other establishment related to herbal infusions [3]. In Turkey tea is a habitual nutrient of Turkish people and cultivated in the east region of the Black Sea. Also, in terms of production and consumption of herbal tea, Turkey is located in the top 10 in the world [4]. In the UK, about 0.5% of annually adverse drug reaction reports received by Medicines and Healthcare Products Regulatory Agency are related to herbal products [5]. A vast majority of herbal products in traditional medicine are used in the form of tea and it is one of the most preferred herbal remedy around the world due to its aroma, favorable taste, stimulating effects on nervous system, and health-boosting effects [6]. The most consumed type of tea is made by brewing the dried leaves of the plant *Camellia sinensis*. This tea can be grouped into three types according to its oxidation level: green tea (non-oxidized), oolong tea (partially oxidized), and black tea (oxidized) [7]. Almost all types of herbal teas are rich in phenolic compounds and people are advised to include these products in their daily diet as health promoters due to the important antioxidant activity of these teas. Showing considerable diversity in their structure, phenolic compounds give physical and chemical properties to tea such as color, flavor, and taste-related characteristics such as astringency and bitterness as well. In addition to polyphenolic compounds, essential oils are another key component of herbal teas; moreover, these teas are reported to contain some other essential compounds such as vitamin A, B6, C, and E [2]. On the other hand, tea polyphenols showed a preventive action against radiation induced haematological alterations in mice [8] and recent epidemiological studies suggested that tea polyphenols are effective even for the prevention of cancer and cardiovascular diseases. Furthermore, it has been shown that some green tea extracts and flavonoid-enriched fractions of Rooibos tea (*Asphalathus linearis*) can have pro-oxidant activities. In regard to health promotion, it is important to draw attention to the fact that potent antioxidants can display pro-oxidant activities which lead to an oxidative damage of cellular components [9].

Owing to the increase in the use of herbal teas all over the world during recent years [3], numerous studies have been conducted on health benefits of herbal teas; however, only few data are available regarding the relationship between herbal tea consumption and blood-related abnormalities [10]. The articles in the published literature often present conflicting findings on the relationship between herbal tea consumption and blood-related parameters such as the degree of iron absorption, serum ferritin concentration, thrombocyte level, and aggregation rate. In this review, we aim to recompile the limited research on the relationship between traditional or habitual consumption of herbal tea and blood-related abnormalities.

Thrombocytopenia

Thrombocytopenia is a bleeding disorder in which the blood contains an abnormally low count of functional thrombocytes [11].

However, there is quite limited information about the causative relationship between the consumption of products related to the herbal teas and thrombocytopenia. An available report on this issue suggests that green tea is wealthy of polyphenolic compounds and the green tea catechins (GTC). The vast majority of beneficial effects of green tea are associated with the GTCs due to their antioxidant, antiproliferative, anti-inflammatory, and antithrombotic activities [12]. According to a case report of Liatsos et al. [13], a 38-year-old woman developed thrombotic thrombocytopenic purpura after consuming of a weight-loss product for two months, which contains green tea extract. The daily preparation supplied by a pharmacy was containing 200 mg of green tea extract which is equivalent to 1 g of natural green tea. The results of laboratory test revealed the marked thrombocytopenia on the admission date and platelet count was 13 folds lower than the normal value and haematological parameters such as hematocrit, hemoglobin level, reticulocyte count, and erythrocyte sedimentation rate were also abnormal. Also, higher level of immunoglobulin G (IgG) autoantibody against ADAMTS13 was detected. The extended anti-metalloproteinase activity of catechins may be the reason of inhibition of ADAMTS13. This case was evaluated as "possible" relationship with green tea consumption according to Naranjo scale of causality; however, there is no similar report associated with green tea induced thrombocytopenia [13].

Another case about thrombocytopenia is reported as a result of using *Echinacea pallida* and leaving the treatment after two weeks of use. Thrombocytopenia, hemolytic anemia, and seizure was reported in this case as well [14]. Moreover, Echinacea is likely to have contributed to the profound thrombocytopenia of an etoposide-treated patient and it is suggested that Echinacea should be avoided in patients receiving chemotherapeutic drugs which are CYP 3A4 substrates since the CYP 3A4 inhibits the potential of Echinacea. Due to the fact that patients receiving chemotherapy become immunosuppressed, it is predictable that some patients may try to self-medicate themselves with Echinacea during treatment to prevent infections and other complications [15].

Several factors increase the risk of thrombocytopenia: type of blood group, ethnicity [16], being older than fifty [17], the use of anti-cancer drugs [18], HIV infection, and heavy alcohol consumption. Development of secondary thrombocytopenia level is greater especially in pregnant women. Although green tea is highly recommended by many physicians since it is considered safe, the consumption of green tea/green tea preparation may give rise to a haematological anomaly [13]. In order to preclude any undesired consequences related to herbal tea consumption, patients and population which is under the risk should avoid the use of these kind of products.

Procoagulation and Prothrombotic Effects

Procoagulant activity plays a key role in atherosclerosis, myocardial infarction, and hypertension while pulmonary thrombosis and platelets accelerate the development of these diseases through participating in thrombosis directly by forming aggregates or indirectly by promoting the coagulation pathway [19]. Few studies have focused on herbal tea product consumption and coagulation dysfunction. Nevertheless, it is important to know the potential prothrombotic effects of herbal products to eliminate the procoagulation risk especially for patients with cardiovascular disease. Song et al. [19] studied on dipsacus saponin C (DSC) which is the active ingredient of well-known anti-inflammatory and analgesic *Dipsacus asper* (DA) herbal tea. They suggest that crude extract of DA can enhance thrombosis at ≥ 50 mg/kg while DSC was more potent and enhance thrombosis at ≥ 10 mg/kg. These exposure levels were in a proximate range from the daily intake when DA is taken as herbal tea (~10 mg/kg for adult), suggesting that increased thrombosis might occur [19].

Serum Ferritin Levels and Iron Absorption

Iron deficiency is the most frequent micronutrient deficiency around the world. Major cause of this deficiency is the impaired absorption of non-heme Fe (3^+) due to the potent inhibitors of its absorption. Polyphenolic compounds are crucial inhibitors of Fe (3^+) absorption since they can form a complex with Fe in intestinal lumen during digestion, which counteracts iron absorption [20]. The inhibition of non-heme iron absorption related to polyphenolic compounds is well-known; however, there are controversial studies in the literature as well. Excessive habitual consumption of tea may lead to marginal iron status in individuals who can develop iron deficiency, especially in children and pregnant women [10]. In contrast to the detrimental findings on herbal tea consumption and iron status, some studies suggest that there is no significant relationship between tea consumption and serum ferritin level [21]. Despite the many cases on the ferritin, which is the most investigated haematological parameter, there are hardly any cases related to herbal tea induced thrombocyte anomaly [13]. In another case, prothrombotic risks were revealed arising from the consumption of herbal tea [19].

According to a population study, the mean serum ferritin concentration has no relationship with the consumption of herbal, black, and green tea in both men and women (pre or post-menopausal) [21]. Temme et al. [22] suggest that there is no relationship between tea consumption and iron status in Western populations. Moreover, it is suggested that there is no need to any restriction on tea consumption in healthy people with no risk of iron deficiency [23] and people with risk of iron deficiency. Moreover, the risk of iron depletion is found not to be related to the variables such as any types of tea, the strength of tea, the consumption time of tea, and infusion time [24]. In contrast to this study, Zaida et al. [25] suggest that tea and vervain infusions, often used in infant diet in Morocco, can contribute to iron deficiency by inhibiting iron bioavailability according to *in vitro* model of digestion both at gastric pH 2.5 (represents the first week of life) and pH 4 (early infant).

In the present study, mint tea showed an improvement on iron bioavailability while the addition of vitamin C contributed to the struggle against the inhibition of iron absorption. Furthermore, iron absorption was higher at low gastric pH when compared to high gastric pH. In the light of this study, it can be suggested that the addition of vitamin C to tea or vervain infusion and the consumption of fresh orange juice instead of tea may protect the weaned babies against the iron deficiency, one of the most common reason of growth and developmental impairment.

The effect of mint tea on iron bioavailability is still questionable since Akdogan et al. [20] suggest that *M. Piperita* tea caused a decrease in serum ferritin and iron levels of rats in a dose dependent manner. Besides these parameters, unsaturated iron-binding capacity (UIBC) showed an increment. On the other hand, another kind of mint tea *M. Spicata* showed no significant effect on serum ferritin, iron, and UIBC [20]. Therefore, the present contradiction should be taken into consideration before drinking mint tea especially when infants, children, and anemic patients are the issue.

Red Blood Cell (RBC) Destruction

Benjamin et al. [26] suggested that normal human red cells incubated with saline extracts of tea may lead to the paroxysmal hemoglobinuria-like defects and incubation with tea may alter the red cell membrane. In the same study, they supported their hypothesis with a case which reports that a young male developed an acute limited intravascular hemolytic episode after ingesting excess amount of herbal tea [26]. *Aristotelia chilensis*, which is traditionally consumed, was reported to induce an alteration of human erythrocyte morphology [27]. Furthermore, another popular product, leaf extract of *Gingko biloba*, exhibited damage to RBC by increasing cell fragility, altering cellular morphology and methemoglobin production, especially when used at high doses [28]. The various adverse drug reactions related to the consumption of herbal tea products have been increased; moreover, the uncontrolled consumption of these products may lead to an increase in the vulnerability of chronic patients or patients treated with chemotherapy [14,29,30]. Nevertheless, the adverse reactions with haematological consequences have been rarely described. Few herbal tea interactions are reported to have haematological consequences in the literature. These interactions are summarized in Table 1.

Herbal Tea	Drug interaction	Effect	Ref
Green tea	Warfarin	Decrease in the anticoagulant effect	Staines [29]
Echinacea	Etoposide	Thrombocytopenia	Bossaer et al. [15]
Gingko	Warfarin	Increase in the anticoagulant effect	Staines [29]
Gingko	NSAIDS	Increased risk of bleeding	Staines [29]
St. John's Wort	Fluoxetine	Thrombocytopenia	Royer et al. [14]
St. John's Wort	Warfarin	Decrease in the anticoagulant effect	Staines [29]
Madagascar rosy periwinkle	Cancer Chemotherapy	Neutropenia of short duration	Kamsu et al. [30]

Table 1: Herbal tea related interactions of haematological concern in the literature.

Effects on Immunological Parameters of Haematopoietic System

Herbal products are increasingly used all around the world to enhance the general well-being and to facilitate immune system. Clinical studies provide empirical evidence that the herbal products can modulate the immune system; however, the mechanisms of this modulation have not been clarified yet [31].

Echinacea purpurea is one of the most used herbal tea for the purpose of immune enhancement mainly in Russia and other countries. Echinosol which is the active ingredient of Echinacea tea is found to be effective on immune response by stimulating the formation of antigen specific T lymphocytes and mature T lymphocytes- and by increasing the number of monocytes and neutrophils in the blood. Furthermore, echinosol is found to be effective on the increment of immunoglobulin (Ig) synthesis during the production phase of immune response [32]. In several studies, beneficial effect of Echinacea on immunity was discussed from a similar aspect [33-35]. In contrast to these studies, *E. purpurea* did not show any significant effect on both mitogen-stimulated and alloantigen stimulated lymphocyte proliferation [31]. According to a study conducted on human T-cell leukemia cell line, isolated dienone from the roots of *E. pallida*, another type of Echinacea, exerted a dose-dependent cytotoxicity [36]. Besides, *E. pallida* was found to be ineffective when immune parameters are concerned in a rabbit study [37].

Popular herbal teas in native South Africa and around the world, Rooibos (*Aspalathus linearis*) and honeybush (*Cyclopia intermedia*) are employed as a folk remedy. According to McKay et al. [38], the effects of rooibos tea on immune system are based on antigen-specific antibody production. Immunomodulating effect of honeybush is attributed to the active ingredient, the mangiferin, which is found to be effective as immunomodulator by inducing proliferation of murine lymphocytes at optimal dose *in vivo* and *in vitro*. In the literature, there is no evidence based on human data about immunomodulating effects of both rooibos and honeybush tea consumption; therefore, immune-boosting usage and toxicological concern in human remain as a question.

The effect of another frequently consumed herbal tea, the green tea, on immune system was also examined by Farahat et al. [39]. According to this study, feeding broiler chickens on diets supplemented with green tea extract resulted in a significant increase in the antibody response against Newcastle disease virus vaccines in comparison to those fed on the control diet [39]. Also, decaffeinated green tea extract showed an immunomodulatory effect on *Oncorhynchus mykiss* fish immune system when administrated in lower doses [40]. In contrast to these studies, green tea extract has been found as immunosuppressant by inhibiting IL-2 production and decreasing IL-10 production in mixed lymphocyte culture *in vitro* and by suppressing proliferation of murine lymphocytes *in vitro* [31]. Due to the inconsistent results and limited human data, mechanism and risk/benefit ratio of herbal tea products as immune-booster are still not clarified in terms of haematological aspect.

Discussion

The most common belief among the population about the "harmless" and "natural" herbal teas and their products lead to the unconscious and extravagant consumption of these products. Excessive consumption of herbal tea and products may lead to serious consequences on blood cells in terms of their function, proliferation rate, and structure as described previously in this review.

Herbal teas differ from synthetic medicines in terms of having chemically rich and complex compounds which are not isolated single active ingredients. Therefore, many different factors can influence the chemical profile of herbal teas both in qualitative and quantitative manner such as parts of the used plant, harvesting time, storage, processing, and geographical origin etc. [5]. The other important key points about this issue are the duration of exposure to the herbal tea, the dose and the co-administrated medicinal or herbal therapeutics since high doses of herbal tea products can be toxic for the cells, not only when used alone but also used with possible interactions as well. Consumption of herbal preparations and drugs together may lead to adverse haematological consequences [14]. Furthermore, they can be used unconsciously around the world due to the common belief about the "harmless" nature of herbal teas. Besides, herbal tea products used to treat clinical conditions are often purchased online without the supervision of healthcare professionals [41] and commercialized easily due to the widespread and accessible "information" *via* internet [42].

In conclusion, it is difficult to define "cause and effect" relationship between herbal tea consumption and changes in haematological parameters. However haematological abnormalities may arise during the consumption period of these products according to the previous reports. Therefore, further research and evidence-based information are necessary to get a better understanding and quantify the contributions of active ingredients of herbal tea products responsible for the blood-related anomalies. Healthcare organizations and regulatory agencies should create detailed dietary guidelines including recommendations for generous intakes of herbal teas and their products. So, excessive or unconscious consuming of these products may mislead public. Also, a punitive sanction or regulation might be preventive against uncontrolled marketing these products online or by the help of exaggerated TV commercials and it is necessary to put this class of therapeutics on the same evidence-based reference as medical therapeutics. Furthermore, continuing educational programs on the consumption of herbal tea and related products should be offered to healthcare professionals as well.

Acknowledgments

Special thanks to Hande Sevgi for her kindly contribution.

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