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Herbal medicine use in patients seeking treatment in emergency departments

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ABSTRACT

To ascertain the extent of toxicological profiles around their medical use, herbal medicine use problems need to be consistently traced for consumer safety. Medical information regarding botanical use in various diseases or disorders, as well as adverse/toxicological effects of the botanicals, was sourced from scientific databases. Patients who request medical care at hospitals may be using at least one formulation of botanicals at the time of the visit, and some of the used medicinal plant products possess the potential to be the cause of toxicity as well as herb–conventional drug interactions. Emergency healthcare providers must be aware of some potential adverse events that may be seen in admitted emergency department patients when the herbal medicine is used alone or concomitantly with conventional medicine. Moreover, emergency healthcare providers must be knowledgeable of herbal medicine practices to ensure that optimal treatments will be selected for these patients.

Keywords: adverse effects; alternative treatments; emergency; medicinal plants; toxicity

1. INTRODUCTION

In many Asian countries, including Thailand, herbal and dietary supplement products are extensively used. In general, in the Asian population, the herbal use prevalence of these products ranges from 22% to 77% (Tangkiatkumjai et al., 2013). The products have been used for health promotion and management of disease conditions such as cardiovascular diseases, diabetes, and cancer (Riewpaiboon, 2006; Tangkiatkumjai et al., 2013). At present, medicinal plants are very popular as traditional household remedies in Thai society. Many herbal/dietary supplement products are distributed in Thai markets and drug stores. The most popular products used among the Thai people are also adaptogens (Sumngern et al., 2011). They contain some phytochemicals that are presupposed to assist the body in adapting to stress as well as encourage or revive regular metabolic/physiologic functions and balance (Sumngern et al., 2011). The increased use of herbal/dietary supplement products is due to several factors, including the requirement for self-health care, perceptions of safety, ease of accessibility, and low cost (Grazina et al., 2020). In fact, herbal/dietary supplement products may not be safe

and may cause serious adverse events due to the utilization of these products, such as blood pressure fluctuation, hepatotoxicity, rhabdomyolysis, and anaphylactic reactions (Saokaew et al., 2011). These are the reasons: It is important for medical staff to have knowledge of herbal/dietary supplement product usage and should have the ability to assess and inform patients on herbal/dietary supplement product usage in combination with conventional therapy. Considering the potential risks of various herbal/dietary supplement products on usage, the product used by patients should be inquired on a regular basis as well as the patient's counseling should be provided (Wierzejska, 2021).

Patients who request medical care at hospitals may be using at least one formulation of herbal medicines at the time of the visit, and some of the used medicinal plant products possess the potential to cause toxicity as well as herb–conventional drug interactions. An emergency department is one of the places in a hospital where users of herbal and dietary supplement products receive conventional therapy. Investigating the use of herbal formulation among patients in a hospital setting, such as an emergency department, will provide information about the burden of herbal formulation-related hospital visits. This will advocate for preventing adverse events related to the use of medicinal plant products (Jatau et al., 2018).

2. HERBAL MEDICINE USE IN EMERGENCY DEPARTMENT

Up until now, there has not been a lot of research regarding utilization of herbal medicines in emergency departments. In a study published by Hung et al. (2008), the prevalence of herbal preparation use among 623 participants from 2,473 eligible acutely ill or injured adult patients who presented at the emergency department of Bellevue Hospital Center, New York, United States, showed significant values. Among the patients who participated in this study, the total prevalence of herbal preparation utilization was 21.7%. Moreover, women were more liable to utilize the products than men (28.5% and 17.2% respectively). Asian patients exhibited a significantly higher utilization value than the white, Hispanic, and black patients. Educational level, employment status, age, and HIV positivity were not significantly involved with medicinal plant preparation and utilization. The medicinal plant formulations of goldenseal tea, garlic, and ginger were most commonly reported in this study. Several of the herbal preparations used have been involved with reported severe systemic toxicity. The prevalence of herbal product utilization among adult patients (≥18 years old) visiting the emergency department remains significant. Therefore, a history regarding individual herbal medicine use may provide useful information about herbal preparation induced toxicity. In a study published by Weiss et al. (2001), one of the objectives of the research was to describe the extent of complementary and alternative medicine (CAM) (focusing on herbal medicines) use among 350 emergency department patients recruited in the study. They performed a convenience sampling of patients presenting in the metropolitan emergency department. Forty-three percent of the subjects had occasionally used CAMs, and twenty-four percent were using CAMs at the present time. The most regularly used CAMs (which were medicinal plant products) were ginseng (13%), *ginkgo biloba* (9%), and St. John's wort (6%). Sixteen percent of the patients considered all CAMs to be safe. Moreover, only sixty-seven percent of them would tell the doctors regarding their CAM uses. Commonly used CAMs should be considered by emergency medicine providers who should routinely query patients in physical examinations regarding their uses of these herbal products. The study published in 2004 by Li et al. (2004) regarding characterization of the CAM utilization of among the 356 patients of the emergency department of the University of California, San Francisco Medical Center. This study demonstrated regarding healthcare utilization patterns among CAM users and non-CAM users using a cross sectional observational study and the results were obtained by administering questionnaires and statistical analyzing. The results regarding herbal uses of the patients demonstrated that of the 356 patients surveyed, seven and two percent of the subjects had tried herbal medicines and megavitamins/dietary supplements, respectively due to presenting medical problems. The number of emergency department visits over the past 12 months did not differ between the CAM users and non-CAM users, but those using CAMs did have more visits to outpatient physicians (7.8 vs. 5.2%). The most frequently used CAM overall in the past year were herbs, which the value was twenty four percent. Regarding megavitamins/dietary supplements, the value was fourteen percent. The most regularly used herbs were Chinese herbs, herbal tea, Echinacea, and ginseng, whose values were 7%, 6%, 5%, and 2%, respectively. Forty-five percent of CAM users have mentioned their use of the therapy to physicians. Another study in the United States was performed by Geller et al. (2015) and published in 2015. The number of emergency department visits that were on account of adverse events from utilization of dietary supplement products, for example, herbal products, complementary nutritional products as well as micronutrients, which included vitamins and minerals regularly utilized in the United States, was estimated using nationally representative surveillance data from 63 United States emergency departments obtained from 2004 until 2013. Moreover, the patients, products, and adverse event types were also identified with their associated characteristics. Based on estimation of 3,667 cases of patients, adverse events due to dietary supplement products resulted in 23,005 emergency department visits in a year. These emergency department visits caused annually an approximate 2,154 hospitalizations. Young adults (20–34 years old), and unsupervised children were frequently involved in such visits (28.0% and 21.2% of visits, respectively). When the visits of unsupervised dietary supplement ingestion by children were excluded, and the visits due to single supplement involving adverse events were considered. The visits associated with herbal/complementary nutritional products, micronutrient products weight loss products and energy products were 65.9%, 31.8%, 25.5% and 10.0%, respectively.

The weight-loss or energy products were the cause of 71.8% of the adverse events associated with tachycardia, palpitations as well as chest pain (cardiovascular manifestations), and 58.0% of cardiac symptoms visits associated with young adults. Among adults aged 65 and over, swallowing problems were common causes of supplement-induced emergency visits, such as choking, pill-induced dysphagia as well as globus that caused 37.6%

of all emergency department visits, which micronutrient products were associated in 83.1% of these visits (Geller et al., 2015).

The study in Asian populations was conducted by Tse and Lau (2007). Traditional Chinese medicines are widely used in Hong Kong. Nevertheless, there is not sufficient rigorous evidence existing on its prevalence among patients seeking medical care in an emergency department. They performed a prospective survey for investigation of the prevalence, the type of used traditional Chinese medicines, frequency, and nature of traditional Chinese medicine-related adverse reactions. The 21,475 patients of accident and emergency department at the United Christian Hospital were scrutinized for traditional Chinese medicine uses and medicine types in a consecutive thirty-one-day period. They also assessed the causal relationships between the traditional Chinese medicines and their exhibiting illnesses. The result showed that 291 emergency patients (1.4%) reported traditional Chinese medicine uses within a one-week period. Among these patients, 117 patients (40.2%) utilized Chinese herbal medicines, 75 patients (25.8%) utilized proprietary Chinese medicines, 1 patient (0.3%) took both medicines, 96 patients (33.0%) received topical treatments and 2 patients (0.7%) were unclassified, with 22 out of the 291 traditional Chinese medicine consumers (7.6%) presented for toxicity associated with the medicines. Experiencing dermatitis after topical medication and allergic reaction after oral administration (68.2% and 22.7%, respectively) were most complications, which were mild.

The cross-sectional study of Turkish populations was conducted by Koc and Cinarli (2018) to investigate utilization of CAM in patients seeking care at the emergency room of Ondokuz Mayis University Training and Application Center Emergency Service. Data was collected from 385 patients using a questionnaire during 02 January–31 March 2016. Stomachache, vomiting, nausea, headache, shortness of breath, and urinary symptoms (17.2%, 14.8%, 11.2%, 10.9%, and 9.6%, respectively) were found to be the reasons for seeking care. Ninety four percent of these patients were discovered to utilize CAM therapies as being prayer, herbal medicine/tea, and dietary supplement products (82.3%, 48.6%, and 9.4%, respectively). Moreover, the result also showed that 80.9% of the subjects did not reveal their CAM utilization with healthcare providers. Another cross-sectional study was conducted in Australia by Taylor et al. (2004). The objectives of this study were to investigate the prevalence and type of CAM utilized by the emergency department patients, and to explore subgroups of the patients more likely to utilize CAM, the circumstances for which these medicines were utilized, as well as the prevalence of side effects, including toxicities related to utilization of CAM. The survey of 404 patients presenting at the Royal Melbourne Hospital, a tertiary referral and trauma center was performed between February 2002 and March 2003 using the specifically designed study questionnaire. Fifty patients had utilized CAM therapies on the visiting day, 203 patients had utilized them in a period of the previous week and 275 patients had utilized in a period of the previous year (12.4%, 50.2%, and 68.1%, respectively). CAM users were found to be younger, have better education characteristics and were more likely to be female when compared with patients who did not use CAM. One hundred and three different CAM had been utilized for various reasons. Of all the 1,182 CAM courses taken, 53 courses experienced side effects. One patient suffered, particularly from toxicity due to CAM utilization.

3. PATIENT ASSESSMENT IN EMERGENCY DEPARTMENT AND TOXICITIES OF HERBAL MEDICINES

It is essential to regard the possibility that unexplained emergency signs and symptoms may be related to the use of a medicinal plant/dietary supplement product. Factors that may cause toxic reactions include a dosage as well as preparation of herb/diet(s), the presence of contaminants, the duration of consumption, misidentification of used remedies, consumer's medical problems, and concurrent utilization of prescribed medications (Shaw, 2010). A thorough patient assessment as an herbal/dietary supplement consumer in an emergency department is difficult and time consuming. A large number of patients who are herbal/dietary supplement consumers do not report their uses. Toxicities and reactions to herbal/dietary supplement products may cause signs and symptoms that may mimic other disease conditions (Holleran, 2005; Phua et al., 2009). To avoid subsequent herb–prescribed drug interactions, questions related to herbal/dietary supplement products must be queried (Holleran, 2005). Possible reactions/symptoms caused by herbal products may be seen in emergency departments include:

3.1 Allergic reactions as urticaria, contact dermatitis, angioedema, and hypersensitivity

In 1998, Moss reported allergic reactions could be caused by some herbs (Moss, 1998). A particular example of the herbal product that causes allergic reactions is garlic (*Alllium sativum* L.), which has been extensively utilized in many geographic regions, including Asia and Southeast Asia, due to its culinary and medicinal attributes (Cavagnaro and Galmarini, 2007; Prasad Reddy and Rhim, 2014). *A. sativum* has been evaluated for its potential antimicrobial, immunomodulatory, and anticancer activities. Organosulfur compounds such as allicin and s-allylcysteine are considered to be the main bioactive compounds responsible for blood pressure and dyslipidemia management. Other organosulfur compounds such as ajoene and allicin have been shown to hinder cholesterol synthesis by restraining 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (Bravo-Núñez et al., 2019; Chan et al., 2019). Garlic is widely used for hypercholesterolemia treatment and atherosclerosis prevention. Case reports have emphasized the potentiality that utilization of this herb may provoke allergic reactions (including generalized urticaria, photoallergy, allergic contact dermatitis, pemphigus, angioedema, and anaphylaxis), platelet function, and coagulation alteration (with a possible bleeding risk) and burns (particularly under occlusive skin dressings where fresh garlic is applied on) (Borrelli et al., 2007). The primary allergenic components found in garlic include diallyldisulfide, allylpropyldisulfide, and allicin (Hitl et al., 2021). These substances possess an electrophilic nature, which means they have the capability to engage with nucleophilic functional groups within proteins. This interaction can

lead to the formation of a complex between the allergenic compounds and proteins, effectively acting as allergens. Intake of *A. sativum* by a breastfeeding mother modifies an infant's behavior during breastfeeding. Moreover, *A. sativum* may augment the pharmacological activity of anticoagulants (such as warfarin and fluindione) by inhibiting Cytochrome P450 and decrease the efficacy of anti-HIV agents (saquinavir) by inducting intestinal P-gp (Bordes et al., 2020; Borrelli et al., 2007; Leite et al., 2021).

In a study recently published by Armentia et al. (2020), they conducted an observational cross-sectional study to determine allergic sensitization and clinical symptoms related to consumption of garlic and onion in 8,109 allergic patients of all ages seeking medical care at their university hospital allergy clinic during the year of observation (2018). They examined 44 aeroallergens and foods that included garlic and onion. Many prick tests and specific IgE determinations were conducted. The results showed that of all subjects tested, 2,508 (30.92%) presented with symptoms related to the consumption of food and, among these subjects, food hypersensitivity was observed by prick test, positive specific IgE or provocation in 924 patients, and was on account of garlic or onion consumption in 27 patients, pointing out a prevalence of 2.92%. A relation between the symptoms and a specific lipid transfer protein to the garlic or onion bulbs was shown by immunodetection. Therefore, this study provides information that health professionals should be aware of allergic hypersensitivity caused by garlic and onion.

Many conventional Chinese medicines, including Chinese materia medica (CMM) injections, can produce type I hypersensitivity reactions (Shi et al., 2022). For example, Shuanghuanglian injection (SHLI), which is mixed from the extractions of *Lonicerae japonicae Flos*, *Scutellariae baicalensis* and *Fructus forsythiae* (Gao et al., 2018). It has found extensive application in the treatment of respiratory tract infections caused by various viruses and bacteria such as pneumonia, tonsillitis, and other respiratory diseases in China. The significant number of severe anaphylactic reactions caused by SHLI led to the Chinese National Medical Products Administration (NMPA) issuing a warning about allergic shock and prompting SHLI to modify its instructions in 2018. The research conducted by Li and colleagues using a rat model (Li et al., 2010) to investigate SHLI induced anaphylaxis has been carried out. Following the sensitization to SHLI, there was a notable rise in both total IgE levels and IgE levels specific to SHLI. After the SHLI administration, various manifestations were noted, including increased levels of histamine, local skin responses, systemic symptoms, and reduced blood pressure. The levels of IL-4, but not IFN-γ, were notably elevated in spleen cells derived from rats sensitized to SHLI. This suggests that the anaphylactic response triggered by SHLI is likely mediated by Th2 immune responses.

3.2 Elevated liver function tests /hepatotoxicity

The toxicity was also reported by Moss (1998). Specifically, one Thai herb has been implicated in hepatotoxicity. Kratom (*Mitragyna speciosa),* which has a widespread distribution in Southeast Asia, such as Malaysia, the Philippines, including Thailand. Kratom preparations are used in Thailand for indigenous medical treatment of cough, worm infections, enteritis, chronic musculoskeletal pain, diabetes, and hypertension (Pantano et al., 2016).

Two cases of hepatotoxicity due to consumption of kratom have been reported by Pantano et al. (2016). The first case was a 25-year-old man, who after two weeks consuming kratom exhibited jaundice and itching onsets. Transaminases, alkaline phosphatase, and direct bilirubin levels were elevated. In the patient's urine sample, a monoterpenoid indole alkaloid; mitragynine as well as the main metabolites were found. Their presence in the sample may be involved in a prolongation of the substance half-life (4 to 9 hours after a single dose in rats), that could be the aftereffect of the hepatic injury. Moreover, a correlation between the *M. speciosa* extract administration and the increased glutathione-S-transferase level in an animal model (mice) has been demonstrated as a plausible sign of hepatic disease. In another case, a 58-year-old man who had jaundice and dark urine symptoms after elongated everyday consumption of kratom extracts was admitted to the hospital. The patient had concurrently taken other conventional medicines (quetiapine and sertraline with the dosages of 100 and 50 mg/day, respectively, for more than two years). A total bilirubin, alanine transferase, aspartate aminotransferase, and alkaline phosphatase levels were elevated that pointed out cholestatic injury. The results convinced the association of the injury with the consumption of kratom (Pantano et al., 2016).

The United States Pharmacopeia has recently finished a thorough and extensive systematic review on green tea extracts (GTE) as part of their continuous evaluation of dietary supplement safety data. Although GTEs have the potential to contain traces of hepatotoxic solvent residues, pesticide residues, pyrrolizidine alkaloids, and elemental impurities, no evidence linking these substances to liver injury caused by GTEs was discovered during the review process (Oketch-Rabah et al., 2020). The review showed that the composition of catechins in GTEs can vary considerably depending on the manufacturing methods employed. Both animal and human studies suggest that when GTE is administered orally repeatedly in large doses and on an empty stomach, there is a significant enhancement in the bioavailability of catechins, particularly EGCG. This effect may be attributed to the potential saturation of first-pass elimination mechanisms. Toxicological investigations reveal that liver injury caused by this substance exhibits a pattern specific to hepatocellular damage. Reports documenting negative effects on the liver have been published, connecting the consumption of EGCG at doses ranging from 140 mg to approximately 1000 mg per day. Furthermore, these reports indicate a significant variation in susceptibility among individuals, which may be influenced by genetic factors (Oketch-Rabah et al., 2020).

Unsaturated pyrrolizidine alkaloids found in plants like Senecio and Symphytum species, including comfrey (*Symphytum officinale* L.), serve as another illustration of herbal substances that can harm the liver. Prolonged consumption of these substances leads to a distinct form of liver damage known as veno-occlusive disease, characterized by the blockage of central and sublobular hepatic veins, which can ultimately advance to cirrhosis (Shaw, 2010).

It was documented that the use of traditional medicine consisting of individual herbal remedies, specifically the

leaves of *Cassia siamea*, was linked to liver damage. In 1999, the initial notifications of liver function irregularities were received, and these reports escalated to a total of 15 cases involving patients with no prior history of hepatitis and who tested negative for the hepatitis B antigen. These individuals experienced liver damage while using the aforementioned product in 2001. Consequently, the risk associated with this product was assessed and communicated to healthcare professionals nationwide. The subcommittee for pharmacovigilance advice suggested a temporary halt in the use of the medication suspected to contain *Cassia siamea* (leaf). Ultimately, the manufacturer voluntarily ceased the product for safety evaluations and additional research. Several investigations were carried out to examine the toxicity of "barakol," whether in its chemical form or as a prepared substance. The findings revealed that the preparation of *Cassia siamea* leaves and barakol induced hepatotoxicity in a manner that depended on the dosage administered (WHO, 2017).

3.3 Cardiotoxicity

Natural cardiac glycosides such as digoxin, digitoxin, and digitalin are a cardiac medication (for treatments of arrhythmia and cardiac failure) obtained from Digitalis, a group of approximately 20 plant species known as foxgloves. Intoxication from Digitalis can also arise from the consumption of these plants, especially in cases of drug overdose. Accidental ingestion is frequently the case, often resulting from the confusion between foxglove leaves and comfrey leaves when preparing tea (Brown, 2018; Vithayathil and Edwards, 2016). Comfrey (*Symphytum officinale* L.) is a perennial plant which has been in recorded use in the practice of Western herbal medicine as an anti-inflammatory and vulnerary for wounds, joint disorders, bone fractures, inflammations, sprains, bruises, pulled muscles and ligaments, and hemorrhoids. (Frost et al., 2013). A case of the accidental toxic ingestion from the confusion has been reported by Vithayathil and Edwards (2016). A previously well-sixty-three years old woman presented to the hospital emergency department in the UK with vomiting, palpitations, and three presyncopal episodes. This patient had no previous medical or cardiac history, with the patient stating that the patient tried an herbal remedy of boiled comfrey leaves for insomnia (by recommendation of the patient's friend) 18 hours before arrival to the department. The ECG showed bradycardia, second-degree atrioventricular node block, Mobitz Type 2, a shortened QT interval, downsloping ST depression and presence of U waves. When the comfrey and foxglove images were considered by the patient, the observation indicated the possibility of mistaken consumption of the foxglove plant, leading to Digitalis toxicity. The comfrey plant closely resembled Digitalis. It is very difficult to distinguish between the leaves of both plants. The patient was not confident which leaves she had purchased from the market stall when both images were shown. Raised serum digoxin levels confirmed this. The patient was hemodynamically stable and given digoxin-binding antibodies. After five days of cardiac monitoring, the ECG of this patient returned to normal rhythm, and the patient was discharged home. Digitalis toxicity can affect cardiovascular, gastrointestinal, as well as visual systems. Arrhythmia with atrioventricular dysfunction is one of most common cardiovascular manifestations. Palpitations, syncope and dyspnea are also seen as associated symptoms. Nausea, vomiting, and abdominal pains are the most common gastrointestinal manifestations. Yellow-green visual disturbances, decreased photophobia, and snowy vision can be seen in patients. Therefore, important for all emergency health care providers to be vigilant of digitalis ingestion in patients with clinical manifestations including nausea, vomiting, and cardiac arrhythmia, together with a history of herbal use (Vithayathil and Edwards, 2016).

The roots of the *Aconitum* species in their natural state contain aconitine and various other aconitum alkaloids, which are widely recognized as substances that can be harmful to the heart. Ingesting wild plants or consuming an herbal decoction prepared from the roots of the *Aconitum* species can lead to serious cases of aconite poisoning. These root vegetables have been utilized in the preparation of soups and dishes due to their claimed advantages for overall well-being. In traditional Chinese medicine, aconite roots are employed for their analgesic, anti-inflammatory, and cardiotonic properties. However, it is important to note that these roots are used only after undergoing a specific processing method aimed at reducing the levels of toxic alkaloids. During the processing or preparation of aconite through soaking and boiling, the aconite alkaloids undergo hydrolysis, transforming them into derivatives that are less toxic or non-toxic. Nevertheless, the risk of poisoning is heightened when larger doses (ranging from 50 to 500 grams instead of the recommended 3 to 30 grams per person) are used, and/or used insufficient detoxification process of aconite preparation (such as using raw instead of processed forms). Even if the boiling process is extended, it may not offer adequate protection if larger quantities of raw roots are consumed, exceeding the recommended amounts (Brown, 2018). In China, the majority of aconite poisoning induced by herbs were primarily attributed to the consumption of herbal medicinal wine. Among five hospitals in Hong Kong, there were a total of 17 instances of unintentional intoxication caused by herbs leading to aconite-related effects. The majority of the cases experienced rapid abnormal heart rhythms (tachyarrhythmias), resulting in two fatalities. In one instance in India, a 40-year-old male encountered bradycardia after consuming just eight drops of a homeopathic tincture. In cases where death occurs, it is typically attributed to the collapse of the cardiovascular system, which can be a result of arrhythmias or respiratory failure. The researchers proposed the necessity of alerting the public about the significant risks of severe poisoning associated with the consumption of aconite roots, whether used in cooking or traditional medicine practices (Brown, 2018).

3.4 Bleeding: acute rectorrhagia and hemorrhagic diathesis

Citrullus colocynthis (L.) Schrad is a particular example of the herbal product that causes acute rectorrhagia. *C. colocynthis*, commonly known as colocynth or bitter apple, a plant which has medicinal and nutraceutical values, especially as a hypoglycemic agent. It is widely available in the Sahara and Arabian deserts, as well as tropical Asia. *C. colocynthis* is extensively used in indigenous medicines in many countries; for example, its seeds are used for diabetes treatment, while its leaves are used for jaundice and asthma treatments (Hussain et al., 2014; Schafferman

et al., 1998). In spite of medical benefits, some complications related to the use of *C. colocynthis* have been reported by Javadzadeh et al. (2013). Four patients who had colocynth intoxication with the main clinical feature of acute rectorrhagia were reported. A prominent early symptom was mucosal diarrhea with tenesmus. Three to four hours afterward, the patients serially developed abnormalities such as bloody diarrhea and finally overt rectorrhagia. Mucosal erosion was only observed by colonoscopy, and after 14 days, it was completely resolved. The membranolytic activity of saponins in colocynth may be responsible for the damage of the intestinal mucosa. Emergency health care providers should be aware of the use of this plant as a possible cause of bleeding of the lower gastrointestinal tract, especially in diabetic patients (Javadzadeh et al., 2013).

The seasonal tonic is an herbal infusion comprising tonka beans, melilot, and sweet woodruff. These natural ingredients are rich in coumarins, which possess potential anticoagulant properties and may consequently slow down the coagulation process. The Seasonal Tonic has been the subject of a case report concerning its potential to cause bleeding. In this report, a 25-year-old woman experienced hemorrhagic diathesis, which was characterized by prolonged prothrombin time and partial thromboplastin time, along with significant reductions in clotting factors V, VII, IX, and X (Hogan, 1983; Wong et al., 2012).

3.5 Brain hemorrhage

Some herbal medicines contain coumarins that may have the potential for hemorrhagic complications. These herbs include red clover, dong quai, and Siberian ginseng, which have been using in remedy for perimenopausal symptoms including hot flashes. The hemorrhagic complication related to use of these medicinal plants has been reported by Friedman et al. (2007) in the case of a fifty-three year old female who visited the emergency department. This patient complained of the worst headache ever. The patient's past medical history, personal/family history of hypercoagulability, as well as history of aneurysm, intracerebral hemorrhage, neurologic illness, other intracranial vascular lesion, pulmonary embolism, vein thrombosis, autoimmune disease including lupus, and spontaneous termination of pregnancy were not detected. The patient had been consuming an herbal product as an alternative hot flash treatment (related to perimenopause) for four months before admission to the hospital. The herbal supplement comprised wild yam (*Dioscorea villosa*), black cohosh (*Cimicifuga racemosa*, which comprises salicylic acid having a potential to cause bleeding), red clover (*Trifolium pratense*, a source of natural coumarins that may increase the effects of antiplatelet and anticoagulant agents), dong quai (*Angelica sinensis*, which comprises at least six coumarin derivatives having anticoagulant properties and is reported its potential herb-drug interaction with warfarin), leaf of raspberry (*Rubus idaeus*), vitex/chaste tree (*Vitex agnus-castus*), Siberian ginseng (*Eleutherococcus senticosus*, which is a source of coumarin derivatives, and dihydroxybenzoic acid as an antiplatelet agent), partridgeberry (*Vaccinium vitis-idaea*), and nettles (*Urtica dioica*, its root extract contains natural coumarins having a potential anticoagulant effect). The dosage of two tablets once daily was taken by the patient, concurrently with a multivitamin. All laboratory tests were normal. The herbal medication was stopped after admission. The neurologic exam showed no abnormality. Subarachnoid hemorrhage within a sulcus over the right frontoparietal convexity was shown by a computerized tomography scan. Cisternal subarachnoid hemorrhage was not found, and pathologic arterial or venous lesion was negative. Magnetic resonance imaging pointed out the hemorrhage, but there was no evidence of tumor, ischemia, or other lesion to elucidate a point in this condition. On hospital day number 2, the patient encountered a severe headache that was recurrent. The repeated computerized tomography scan indicated a new hemorrhage area over the left frontal convexity surface. The headache was relieved, and the patient remained neurologically intact. After that, the patient was discharged and did not resume consuming any medicinal plant products. Two weeks later, the patient was followed up by a computerized tomography scan. The result disclosed resolution of all intracranial hemorrhage. A complete and uneventful recovery was made. After that, there was no recurrent hemorrhage over a six months period (Friedman et al., 2007). Medicinal plant products comprising natural coumarins may be possible causes of intracranial hemorrhage, and use of these herbal medications should be aware and considered by emergency medicine providers.

Saw palmetto, scientifically known as *Sabal serrulata*, is a plant belonging to the Arecaceae family. It is native to the subtropical regions of the Southeastern United States. Saw palmetto extract is obtained by processing the fruits and seeds of the plant and has been employed in various traditional herbal and folk medicine practices. Throughout history, saw palmetto berries have been consumed as a dietary staple to alleviate stomach pain and diarrhea. They have also been recognized for their expectorant and antiseptic properties, as well as their ability to stimulate metabolism. Additionally, saw palmetto has been used to treat various conditions such as goiter, anorexia, polycystic ovaries, and has even been employed as a diuretic and sexual tonic. The indigenous peoples of America utilized the fruit both as a food source and as a remedy for a range of urinary and reproductive system ailments. Since the 1800s, medical literature has documented the use of saw palmetto extract as a treatment for providing symptomatic relief in cases of benign prostatic hyperplasia (Anastassakis, 2022).

A case of brain hemorrhage from saw palmetto has been reported by Cheema et al. (2001). The 53-year-old Caucasian male patient with a meningioma located in the left petroclavial region that extended into the midbrain and cavernous sinus was referred to the University of Arkansas for Medical Sciences in order to undergo surgical removal of the tumor. Throughout the surgical procedure, the patient experienced significant and uncontrollable bleeding, despite attempts to manage it by packing with muscle and utilizing avitene and fibrin glue. After administering 4 liters of crystalloid fluids, four units of packed red blood cells, three units of pooled platelets, and three units of fresh frozen plasma, the bleeding eventually ceased. The surgical procedure ended prematurely, but fortunately, the patient experienced a normal recovery without any subsequent complications. The laboratory tests conducted prior to the surgery showed normal results. However, following the procedure, the bleeding time assessment revealed an extended duration of 21 minutes, exceeding the normal range of 2 to 10 minutes.

After a period of two days, the bleeding time reduced to 14 minutes and subsequently returned to normal over the following five days. The patient confirmed not having taken any nonsteroidal anti-inflammatory drugs before the surgery. Upon conducting additional investigations, the patient revealed that he had been using 'saw palmetto' for the management of benign prostate hypertrophy. The patient had not previously mentioned this information to his physicians because he did not consider it significant, assuming that since 'Saw Palmetto' was an herb and not a prescribed medication, it was not necessary to disclose (Cheema et al., 2001).

Saw palmetto extract is widely accessible as an over-the-counter remedy and is manufactured by numerous herbal drug companies (Cheema et al., 2001). The liposterolic extract of saw palmetto contains significant levels of free fatty acids, which exhibit in vitro properties of anti-androgenic activity and inhibition of 5α-reductase (Anastassakis, 2022). *In vitro* and *in vivo* studies have demonstrated that it has the ability to inhibit the activity of cyclooxygenase and 5-lipoxygenase. This mechanism prevents the production of prostaglandins and leukotrienes, which are responsible for promoting inflammation (Anastassakis, 2022; Cheema et al., 2001). There is currently no available data regarding these effects in humans. Consequently, the extended bleeding time observed in this patient is likely attributed to platelet dysfunction caused by the inhibition of cyclooxygenase resulting from the consumption of saw palmetto extract (Cheema et al., 2001).

4. CONCLUSION

As the result of the interest in herbal medicine, those patients who selected these remedies will be admitted and requested for healthcare in an emergency department. The growing trends of herbal consumption will challenge emergency healthcare providers to be knowledgeable of herbal medicine practices to ensure that these admitted emergency department patients receive optimal healthcare.

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