



Available online freely at www.isisn.org

Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973

Journal by Innovative Scientific Information & Services Network



REVIEW ARTICLE

BIOSCIENCE RESEARCH, 2020 17(2): 793-814.

OPEN ACCESS

Medicinal proprieties and toxicology of therapeutic herbal tea: A review

Leila Belfarhi¹, Mustapha Mounir Bouhenna¹, Yesmine Bouafir¹, Ali Zineddine Boumehira^{1,2,3}, Amira Nebbak¹, Borhane Elddine Cherif Ziani¹, Khaloudoun Bachari¹, Daniel Joe Dailin⁴, Ting Ho⁵ and Hesham Ali El Enshasy^{4,6}*

¹Centre de Recherche Scientifique et Technique en Analyses Physico-Chimiques CRAPC. Zone Industrielle, BP384 Bou-Ismaïl, Tipaza, **Algeria**

²University of Algiers 1, Faculty of Sciences, LVBRN, Algiers, **Algeria**

³University of Science and Technology Houari Boumediene, FSB, LBCM, Bab Ezzouar, Algiers, **Algeria**

⁴Institute of Bioproduct Development (IBD), Universiti Teknologi Malaysia (UTM), Johor, **Malaysia**

⁵Global Agro Innovation (HK) Limited, **Hong Kong**

⁶City of Scientific Research and Technology Applications, New Burg Al Arab, Alexandria, **Egypt**

*Correspondence: henshasy@ibd.utm.my Received 27-02-2020, Revised: 18-05-2020, Accepted: 20-05-2020 e-Published: 03-06-2020

Herbal teas or tisanes, like all foods of plant origin, start to take an important consideration in new product development in the recent years. This based on the increased awareness of their health benefits. It's widely known that large number of medicinal plants of are exist world-wide, research in product development of herb teas is limited. However, herbal teas can exhibit also serious negative. Therefore, consumption must be set under some sort of medical control. Other issue is the quality control of herbal teas which govern the decision of the acceptance or rejection of the raw materials and finished products. Quality control methods of herbal teas is not limited to traditional macroscopic and microscopic analysis of the plant but should include new analytical methods such as high performance liquid chromatography, gas chromatography (HPLC), nuclear magnetic resonance (NMR) and many other new analytical tools for qualitative and quantitative analysis of the plant compounds. The latter facilitated the study of herbal teas as well as benefits and risks of on the consumer health. The present review aims at shedding light on the positive and negative effects of herbal teas with particular references to those in the Algerian market.

Keywords: Herbal teas, quality control, risks of herbal teas, benefits of herbal teas.

INTRODUCTION

Plant cells have been used as main source of human diet based on the highly diversified nutritional values as source of carbohydrates, protein, and vitamins (Sarmidi and El Enshasy, 2012). In addition, plant cells are always considered as the first source of enzymes, essential metabolites, functional colors, and bio therapeutic molecules (Malek et al., 2016; Aladdin et al., 2017; El Deeb et al., 2018; Agouillal et al., 2018; Gomaa et al., 2019; Mohamad, 2019).

Therefore, or centuries, herbs have been used for centuries either in fresh or dried form for direct consumption. Herbal teas have been used since antiquity by many civilizations for their healing roles. They were known by ancient Greeks under the name "Ptisan". Herbal teas are classified into two categories: simple and composed. The simple ones contain few constituents and are for everyday uses as cough herbal teas which generally contain lemongrass, cumin and licorice. There are also simple herbal teas that contain

verbena, thyme flowers, peppermint and fennel which relieve the colon from constipation. Composed herbal teas are for therapeutic use and contain so-called effective medicinal plants with many beneficial effects on major functions (Sofowora et al., 2013). For example, the yerba mate tea of Paraguay contains phenols that are able to regress the proliferation of cancer. The responsible mechanism of a such effect implies the inhibition of topoisomerase enzyme (Gonzalez de Mejia et al., 2005). They also have other constituents such as chlorogenic acid, thrombin, quercetin, kaempferole and andrutin which have beneficial effects on the heart, nervous system, kidneys, liver, stomach and pancreas (Heck and De Mejia, 2007). In addition, herbal tea of *Carissa xylopicron* mixed with pieces of guinea fowl wood are used to decrease the fever engendered by thyroid gland diseases. It can also act against pylorus infections. Some herbal teas based on the plant *Poupartia borbonica* are used by women as a contraceptive (Lavergne, 1989). Otherwise, some herbal teas consist of a single plant but they act on several organs. For example, herbal teas based on the plant Kella, *Ammi visnaga*, are useful against gastric hyperacidity ulcer and kidney lethiasis (Jan, 2014). Moreover, herbal teas have other building functions that the body needs in case of deficiency like cola nuts (Lim et al., 2014). This tea was used against fatigue and weakness by the African people due to its richness in starch, reducing sugar, B-catechin, L-epicatechin and theobromine.

However, the use of herbal teas must be controlled since their components can contain toxic elements engendering a possible risk on vital functions especially on those of liver and kidneys (Kane et al., 1995). In case of example, the Kusmi tea contains pyrrolizidinic alkaloids (PA) which are carcinogenic (Schoental, 1982). Though, the chaste tree *Vitex agnus-castus* plant has produced undesirable effects such as the termination of lactation by its binding to the dopamine D2 receptor of the pituitary gland, whereas it has long been present in herbal tea components (Hamilton et al., 2009; Jones et al., 2008). This type of herbal teas must be controlled to prevent their risks to consumers.

Quality control of herbal teas is a lengthy procedure that includes inspection tests that can prove the quality of herbal teas to satisfy the customer. These control methods also contribute to the decision to accept or reject the herbal tea. There are several methods of controlling herbal teas. Quality control methods for herbal teas

include physicochemical and biological analysis. Biological control methods include *in vivo* and *in vitro* tests. The purpose of these tests is to study the therapeutic effects of herbal teas as well as their side effects on living organisms. There are other methods of controlling herbal teas, like macroscopic and microscopic studies of the plant. However, these methods have become old with the appearance of new analytical methods such high performance liquid chromatography (HPLC), liquid chromatography/tandem mass spectrometry (LC-MS), atomic absorption spectrophotometer (AAS) analysis, and nuclear magnetic resonance (NMR). The latter facilitates the study of herbal teas as well as the benefits and risks of their preparations on the health of consumers.

In traditional medicine, herbal teas are prepared on the basis of several plants to relieve complex diseases. Some of herbal teas have similar characteristics and functions (Li et al., 2002). For example, the anti-stress herbal tea is made up by both *Passiflora coerulea* L. and *Eschscholzia californica* Cham which contains chrysin known to have an action against epileptic seizures (Singh et al., 2011). Other herbal teas are formed by the combination of plants with different functions and characteristics so that one improves the effect of the other (Li, 2002).

The methods of formulating herbal teas are numerous including infusion, maceration and decoction, some of which lead to changes in the plant composition (JÄGER et al., 2011). Infusion of *althaea officinalis* inactivates its molecules (mistletoe lectins). The hot decoction processes of certain herbal teas based on *Acacia* concentrate antiviral molecules against the H₁N₅ virus. Other types of herbal teas, like the Chinese herbal tea "Richter", augment the blood pressure due to the presence of the plant *Glycyrrhiza glabra* in the mixture (Heikens et al., 1995). Another example is "Dr. Ming's herbal tea" which is a slimming herbal tea that contains anthraquinone of rubarbe plant known for their carcinogen risks (Blömeke et al., 1992).

In Algeria, it exists a lot of herbal tea brands which attract more and more people searching for alternative solutions to chemical drugs. However, some types of herbal teas are commercialized without controlling of their components. They contain plants which are not included in the list of ingredients (Derouiche and Abdennour., 2017). In this work, we recapitulated the therapeutic effects of existing herbal teas and their constituents. We also shed light on the negative effects of herbal teas with specific regard to those marketed in

Algeria in one hand, and describe methods of control that allow the study of herbal tea constituents and their risks on consumers, on the other hand.

Health benefits of herbal tea consumption

Plants have long been valued by human beings throughout the world for their medicinal properties and tisanes were the only way to heal in ancient times. It is the link with nature that allowed to choose the most useful plants and the way to prepare their herbal teas. Currently, many societies use medicinal plant herbal teas for their therapeutic effects especially in some rural countries in Africa (Joubert et al., 2008). A large gamut of animals and clinical studies suggests that chemical constituents of herbal teas play an important role in human health (Park et al., 2014). Health benefits derived through the consumption of herbal teas are summarized below.

Fight against fatigue and weakness and boost immunity

Interesting example is herbal tea made of cola nuts which is rich with starch, reducing sugar, B-catechin, l-epicatechin and theobromine. The African population used this herbal tea against tiredness and weakness (Lim, 2014). Another example is herbal tea made of the licorice root plant. The latter reduces the rate of cortisol and reduces fatigue and stress (Omar et al., 2012). There are selective herbal teas that act on fatigue through activation of immune system. They contain vitamin C which is essential for building up a strong immune system. For example, "Tearaja tea", a mixture of plants and algae such as *glycyrrhiza glabra* herbs (liquorice) and spirulina which is rich in vitamin C, in calcium and iron that strengthens the immune system (Gershwin et al., 2007), fights fatigue, treats anemia and restores the body. The herbal tea made of *Polygonatum alve-lobatum Hayata* is rich in flavonoids which activate lymphocytes, increase phagocytosis, induce interferon production (Khodadadi, 2015), increase physical activity and fight against fatigue (Horng et al., 2014). Another example, "HEY GIRL Energize tea" contains Oolong tea and Green tea displaying high levels of caffeine which increases the body energy (Muramatsu et al., 1995). It also contains Guarana (*Paullinia cupana*) which is an effective plant against fatigue observed in cancer patients after chemotherapy (Campos et al., 2011).

Reduce obesity

Studies on rats demonstrated that herbal teas made of the plant *Salvia* contain two diterpenes named carnosic acid and carnosol that significantly inhibit the pancreatic lipase activity and delete the increase of serum triglycerides (Hamidpour et al., 2014). Other studies conducted on animals have shown that lavender-based tea decreased serum cholesterol, triglyceride, low density lipoprotein (LDL) and very low density lipoprotein (VLDL) levels (Rabiei et al., 2014). Herbal teas used for the treatment of obesity have replaced the role of surgical operations and drugs. For example, a study in Saudi Arabia showed that the use of herbal teas for weight loss is high. This is due to the effectiveness of herbal teas prepared in this region by plants such as bran; plantain; senna; capicum; ginger, turmeric; fenugreek; flaxseeds and fennel (Eldalo et al., 2017). Other studies have shown that consumption of oolong tea is associated with a significant decrease in body weight after six weeks of use (He et al., 2009). The Chinese tea "xin-juxiao-gao-fang" is widely used in China to lose weight. This herbal tea has a long-term effect (after 24 weeks of consumption) and without side effects (Zhou et al., 2014). Another study has also shown that *rhizome coptidis* based herbal tea has a berberine molecule that reduces weight, lipids level, glycemia and inhibits adipogenesis (Xie et al., 2011). Other studies do not agree with the use of herbal teas because of their complications. The consumption of herbal tea rhizome lotus, green tea and *Panax notoginseng* causes irritation and constipation problems.

Reduce the risk of cardiovascular diseases

Ginger is among the effective herbal teas against cardiovascular diseases. Studies showed that ginger herbal tea is utile for relieving symptoms of platelet atherosclerosis (Vasanthi and parameswari, 2010). In this study, ginger was administered to patients suffering from atherosclerosis. It resulted in a significant reduction of platelet aggregation induced by blood lipids. Another example is the digital plant that contains glycoside, which stimulates heart contraction and treats heart failure (Reddy et al., 2010). Another Clinical study tested the effects of herbal tea Sarasin (*Fagopyrum esculentum*) on patients with chronic venous insufficiency. The study showed that treatment with sarasin tea is safe and can reduce the oedema development, the diameter of femoral veins and the permeability of the capillaries (Ihme et al., 1996). A clinical

study carried out on herbal teas based on *Withania somnifera* (WS) has shown that it reduces the stress incurred by the nervous system and regulates cardiovascular parasympathetic system. According to this study, consumption of this tea increases physical performance and decreases blood pressure, promotes blood circulation and increases oxygen consumption. In a study of an herbal tea formed by the plant *Salvia miltiorrhiza* demonstrated that it relaxes the coronary arteries, reduces the thickness of the intima in the carotid arteries, inhibits platelet aggregation and prevents the oxidation of LDL (Wang, 2010). Tanshinone, cryptotanshinone and Salvianolic acid were isolated from *S. miltiorrhiza* which have protective effects against angina of the chest and myocardial infarction (Yong et al., 2009). Studies have shown that these herbal teas reduce endothelial cell apoptosis and inhibit atherogen (Ling et al., 2008). However, other studies have found that *S. miltiorrhiza* may cause side effects at high doses such as dryness of the mouth, dizziness, lassitude, numbness and shortness of breath (Yong et al., 2009). Interaction of *S. miltiorrhiza* with drugs such as coumadin (Warfarin) increases anticoagulation (Yong et al., 2009). Some types of African herbal tea molecules possess double effect; both toxic and therapeutic at the same time. For example, the herbal tea Nerium oleander contains cardenolides (oleandroside and neriin) which display beneficial effects on the heart despite of their lethal action (van der Bijl and van der Bijl, 2012). Another example is the herbal tea made of the plant *Drimys sanguinea* which has been used in African traditional medicine for the treatment of cardiac oedema, but this plant is also involved in human intoxication (van der Bijl and van der Bijl, 2012). Herbal teas are a danger to the heart because it is a sensitive organ to cardiac arrest. The use of herbal teas for the treatment of cardiac problems must be subjected to medical control and chemical analysis of the constituents.

Heal asthma and respiratory diseases

As an example, the herbal tea based on *Syzygium cumini* relieves early stages of respiratory allergies. Studies have found that *S. cumini* inhibits the release of histamine involved in respiratory allergies (Brito et al., 2007). Another example is the herbal tea brand "life budding" and its ability to relieve respiratory allergies. This herbal tea contains polysaccharides and malic caffeic acid which possesses an anti-inflammatory activity (Hajhashemi and Klooshani., 2013). There

are also herbal teas prepared by *Dahlia* plant. They contain molecules such as two chalcones, 4,2', 4'-trihydroxychalcone and 3,2', 4'-trihydroxy-4-methoxychalcone (Lam and Wrang, 1975). The chalcone molecules reduce airway inflammation to bronchial hyper-reactivity, suppress Th₂ cytokine production from CD₄ T cells and decrease mucus production (Iwamura et al., 2010). Studies conducted on these herbs have unveiled several constituents that have beneficial effects on many pathologies. For example, *combretum* is useful for coughing and colds due to the presence of some molecules namely genkwanin, rhamnocitrin, quercetin-5,3'-dimethylether, rhamnazin, and 5-hydroxy-7,4'-dimethoxy-flavone which have anti-inflammatory activity.

Prevent Diabetes

A recent research showed that the Chinese herbal tea "BXXD" can ameliorate diabetic gastroparesis by adding the motilin, gastrin nitric oxide to plasma. This herbal tea deletes vasoactive intestinal peptide and adjusts gastric myenteric plexus (Tian et al., 2013). The results of another studies reveal that the *Sambucus nigra* herbal tea possesses a hypoglycemic effect. This plant is rich in polyphenols that reduce the level of cholesterol in the blood. By this action, it reduces diabetes complications (Ciocoiu et al., 2009). The effects of acidified methanol elderberry extracts dietary supplementation on diabetic Wistar rats show a reduction in serum glycemia (Salvador et al., 2017). Another example is ginseng tea that increases the sensitivity of blood sugar to insulin (Gui et al., 2016). Dandelion tea has been used for a long time in China for the treatment of diabetes. Studies have found that this plant is rich in antidiabetic molecules such as β -carotene, which protects cells from oxidation and cellular damage. It also contains taraxasterol and taraxinic acid which have antihyperglycemic effects (Wirngo et al., 2016).

Fight against arthritis

The herbal tea based on *Tripterygium wilfordii* Hook F has long been used in China to treat rheumatoid arthritis. This herbal tea has been the subject of several clinical studies. It was reported that the use of this herbal tea in combination with methotrexate has beneficial effects on the evolution of rheumatoid arthritis (Tao et al., 2002). Other clinical studies have found that the decoction of *Tripterygium wilfordii* Hook F developed adverse effects (Cai and Guo., 1974;

Jian and Zhou, 1987). A study has shown that the herbal tea *Guianensis* inhibits the tumor necrosis factor (TNF) production involved in arthritis (Sandoval et al., 2002). Recent studies revealed that WS herbal tea effectively reduces arthritis syndrome without any toxic effect. Another example is the *Cardiospermum halicacabum* herbal tea which was long used in India for the treatment of rheumatism (Chopra et al., 1982). This herbal tea acts on the production of pro-inflammatory mediators like nitric oxide and TNF α (KC and Krishnakumari, 2006).

It was reported that the use of the kinkeliba tea produced from *Combretum micranthum* has been used since 1912 in Africa. This herbal tea was introduced into the French Pharmacopoeia because of the importance of its medicinal virtues. Studies have found that kinkeliba tea has an inhibitory action on the production of nitrite involved in the pathology of arthritis.

Cancer Treatment

The increasing use of herbal teas and medicinal plants by cancer patients and survivors can be seen worldwide (Chen et al., 2008; Deng and Cassileth). They used herbal teas to improve their physical and emotional well-beings and to reduce cancer therapy-induced toxicity (Wong et al., 2010; Wang et al., 2013; Zhao et al., 2014). The chemopreventive effects of green tea intake have been shown in many *in vivo* studies. For the 7,12-dimethylbenz(a)anthracene (DMBA) and 12-Otetradecanoyl phorbol-13-acetate (TPA)-induced skin papillomas, partial tumor regression or > 90% inhibition of tumor growth, and marked inhibition of tumor growth (46–89%) were observed after administration of green tea (Wang et al., 1992). Aqueous extract of green tea inhibited carcinogen-induced lung tumorigenesis in mice by 63% (Wang et al., 1992). Ginseng is another well-studied herb that shows strong chemopreventive activities. In a lung adenoma model induced by 48 weeks of DMBA, it decreased the average diameter of the largest lung adenomas by 23% and the incidence of diffuse pulmonary infiltration by 63%. In the Ginseng treatment group sacrificed 56 weeks after birth (aflatoxin B1 combined with Ginseng), the incidence of lung adenoma (29%) and hepatoma (75%) was decreased (Yun et al., 1983). Oral administration of aqueous extract of red Ginseng decreased tumor multiplicity by 36% and the tumor load by 70% (Yan et al., 2006). Korea White Ginseng (KWG) significantly reduced the percentage of squamous cell carcinoma to 9.1%, compared with 26.5% in the control group.

KWG also significantly reduced the squamous cell lung tumor area to an average of 1.5%, compared with 9.4% in the control group (Pan et al., 2013). Anti-tumor B (ATB), also called Zeng-Sheng-Ping, is a Chinese herbal mixture composed of six plants that has shown an anticancer effect in mouse models of bladder cancer (Fan et al., 1993), lung cancer (Wang et al., 2003; Zhang et al., 2004) and oral cancer (Wang et al., 2013). Preclinical studies have shown that ATB could reduce the incidence of N-butyl-(4-hydroxybutyl) nitrosamide (BBN)-induced bladder cancer by 90.7% (Fan et al., 1993). ATB caused a significant reduction in lung tumor multiplicity and tumor load (40% and 70%, respectively) (Wang et al., 2009). In an oral squamous cell carcinoma model, ATB decreased the incidence and multiplicity by 59.19% and 64.81%, respectively (Wang et al., 2013).

These results suggest that Chinese herbal medicine (CHM) could be a potential chemopreventive agent for cancer. Moreover, the findings from the *in vivo* studies have shown that CHM can exert potent chemopreventive effects against many types of cancer.

Herbal teas, medicinal proprieties, chemical constituents and posology

Herbal teas are classified into two categories, simple and composed herbal teas. The former contains little constituents and they are for everyday use as coughing herbs, constipation and digestion. The second are for therapeutic use and contain so-called effective medicinal plants. Some constituents appear several times in herbal teas. For example, fennel is found in sudorific, diuretic and appetizing herbal teas (Guérin-Méneville et al., 1837). The little holly is found in either simple or composed herbal teas. However, herbal tea preparations and their potential therapeutic applications are summarized in table 1.

Pharmacokinetics and pharmacodynamics of herbal teas in human body

The determination of the effect of herbal teas in the body is still poorly understood.

Table 1: Herbal Teas, Chemical Constituents, Medicinal proprieties and Toxicological effects

Herbal Tea	Medicinal plants	Preparation and Mode of Administration	Posology	Effects on Human and Animal	Complication and Side Effects
Ginseng-like tea (China)	<i>Uraria crinita</i>	Aqueous extract of <i>Uraria crinita</i> Drinking water		Regulate digestive activity, diarrhea, Remove swelling and its antitussive effects. Anti-inflammatory, Antimicrobial, Antidiabetic effect	No reported side effect
Thüringer 9 -Kräuter Tea» (Germany)	<i>Mentha piperata</i> , <i>bramble Rubus fruticosus</i> , <i>camomile Matricaria recutita</i> , <i>balm Melissa officinalis</i> , coriander <i>Coriandrum sativum</i> , sandalwood <i>Santalum album</i> , <i>Citrus aurantium</i> , <i>Krameria triandra</i> and <i>Pimpinella anisum</i> .	1 filter bag for 1 cup, pour over fresh, bubbly boiling water . Brewing time: 8 minutes	1.5g /day	Decrease cyclosporine level after renal transplantation	No reported side effect
Sarasin tea (China)	<i>Fagopyrum esculentum</i>	Infusion	Very small dose	Heart tonic, Reduce the oedema development; the diameter of femoral veins and the permeability of the capillaries	No side effect
Indian winter tea (India)	Ashwagandha	Infusion	120 mg to 2 g /day	Increases the energy and the cardiorespiratory fitness, Improves the number of hemoglobin (Hb) and RBCs	Abortifacient properties
Ma Huang & Guarana	Guarana; éphédra	infusion	72 mg (ephedra) 240 mg (caffeine)/8 w	Decrease in body weight. Reduce hip and waist circulation.	Reduction in serum TG, Dry mouth, insomnia, headache. Cardiac palpitation and hypertension
ARALOX	A compound of <i>Aralia mandshurica</i> (A) and <i>Engelhardtia chrysolepis</i> (E) extracts	infusion	450mg/d	Decrease in total body and fat weight.	Reduction in perilipin content in adipocytes and plasma TG. Stimulate activity of hormone sensitive lipase
Bofu-tsusho-san	<i>Ephedrae Herba</i> , <i>Glycyrrhizae Radix</i> , <i>Forsythiae Fructus</i> , <i>Schizonepetae Spica</i>	Infusion	280 mg /24 w	Exert favorable effects on obesity-related hypertension	Loose bowel movements
Jiang-zhi jian-fei yao: the refined Rhubarb		Injected intragastrically		Reduce food intake, Decreased size of abdominal adipose cells	Acceleration of intestinal movements ; Prolongation of stomach evacuations time.

Little data on the pharmacokinetics and pharmacodynamics of herbal teas, knowledge of their variability, their action on the body, their interactions as well as their mechanisms of elimination are essential to determine in the future their effectiveness as well as their toxicology. The majority of pharmacokinetics studies on herbal tea are limited to certain herbal teas like ginseng tea, curcumin tea or other ordinary and simply herbal teas. The majority of information on the mechanisms of this simple herbal tea is related to their metabolism through enzymes such as cytochromes P450 (CYP) (He et al., 2010). However, studies on complex herbal teas used in popular medicine for treatment of complex diseases are not available. It is necessary to give importance to pharmacokinetic and pharmacodynamic studies to explore other ways. For example, analysis of the Japanese herbal tea yokukansan TJ-54 revealed its action on the glutamatergic and serotonergic nervous systems. This herbal tea also interacts with 5-HT_{1A} receptors. This herbal tea does not take the metabolic way CYP 450 and is not metabolized by the organism because of the absence of CYP2C in human organism (Goldstein et al., 1994). Another example is the herbal tea K-601, widely used in traditional Chinese medicine for the treatment of influenza. However, a study was conducted on volunteers to determine its effects on the body demonstrated that the herbal tea K-601 interacts with the intestinal flora and has no reaction with the respiratory system. This study demonstrates that this herbal tea acts on intestines and thus, generates secondary metabolites like: secologanose, emodin, lotusine, palmatine, berberine and baicalin (Alolga et al., 2015). Studies have shown that molecules such as secologanose have anti-cancer effects (Jiménez-Sánchez et al., 2017). This demonstrates that pharmacokinetic studies of herbal teas can reveal the appearance of new molecules for medical interest. The pharmacokinetic study of the Yokukansan herbal tea unravels other molecules such as glycyrrhizic acid which goes through tractus intestinal and get metabolized in the form of acid 18 β -glycyrrheticin (Kitagawa et al., 2015). This latter induces apoptosis of cancer cells (Lee et al., 2008)

Toxicity risk related to herbal tea consumption

Herbal teas with single effect

Herbal teas are formulated from plants which exercise actions on the ill organs in the human

body and do not have toxic effects on healthy ones. The tisane made of the bearberry plant *Arctostaphylos Uva-ursi* possesses disinfectant actions of urinary tract and lacks toxic effects on other organs (de Arriba et al., 2013). Another example is the herbal tea of *Caralluma fimbriata* which acts against fats without affecting the major function of body (Arora et al., 2015). This type of herbal teas can be employed without having fear of its secondary effects since their components are tolerated by the human body.

Herbal teas with double effect

There are other types of herbal teas with double effect which act against already ill organs and touch healthy ones as it is the case of the slimming herbal tea Ngamrahong. Ngamrahong means « interior wellbeing ». It is made up the plant *Senna* as a main component which is a plant known for its richness with anthronoides (Lemli et al., 1983). They act against mitochondria by diminishing the production of ATP and water retention. According to other studies, Ngamrahong leads to an acute liver failure and renal insufficiency and encephalopathy (Vanderperren et al., 2005). Another example of herbal tea risks is the herbal tea "Richter" having licorice as a constituent. The latter increases blood pressure and engenders complications to all hypertensive people (Heikens et al., 1995). The herbal tea of badiana is used in the form of infusion of dried seeds acting against constipation. It exists varied types such as *Illicium verum* of China criticized for its toxicity and the one of Japon which is extremely toxic. Cases of seizures have been signaled after the use of *Illicium anisatum* of Japon which contain toxic components such as actones sesquiterpenic anisatin, neoanisatin and pseudoanisatin

Quality control of herbal teas

Phytochemical analysis

Despite of the numerous beneficial effects of herbal teas, mainly attributed to their polyphenolic constituents (Sang et al., 2011), they are subjects to some risks and contaminants that occur during growth, development and processing and should be monitored to ensure the safety and the quality of these remedies.

Contaminant risks of herbal teas

The vulgarization of the herbal tea use with for only slogan: "what is natural is harmless" induced a poor quality of herbal products (de Andrade et

al., 2018). However, and contrary to popular belief, not every natural product is exempt of dangerous hazards (Ridker, 1987). For example, it has been demonstrated that products of *Piper methysticum* and *Symphytum officinale* induced serious damages in liver (Mattocks, 1980; Stickel et al., 2003). Since herbal teas are made of roots, leaves, fruits, flowers, seeds or even other parts of the plant like barks, nuts...etc., they are continuously exposed to some toxic and

pathogenic contaminants (Kosalec et al., 2009). Thus, warranting the best quality to the consumer, by proving their medical harmlessness and conformity to standards, is essential. Problems linked to the growing conditions, preparation methods and processing including harvesting, drying and storage can affect the final product safety (Prchalová et al., 2017).

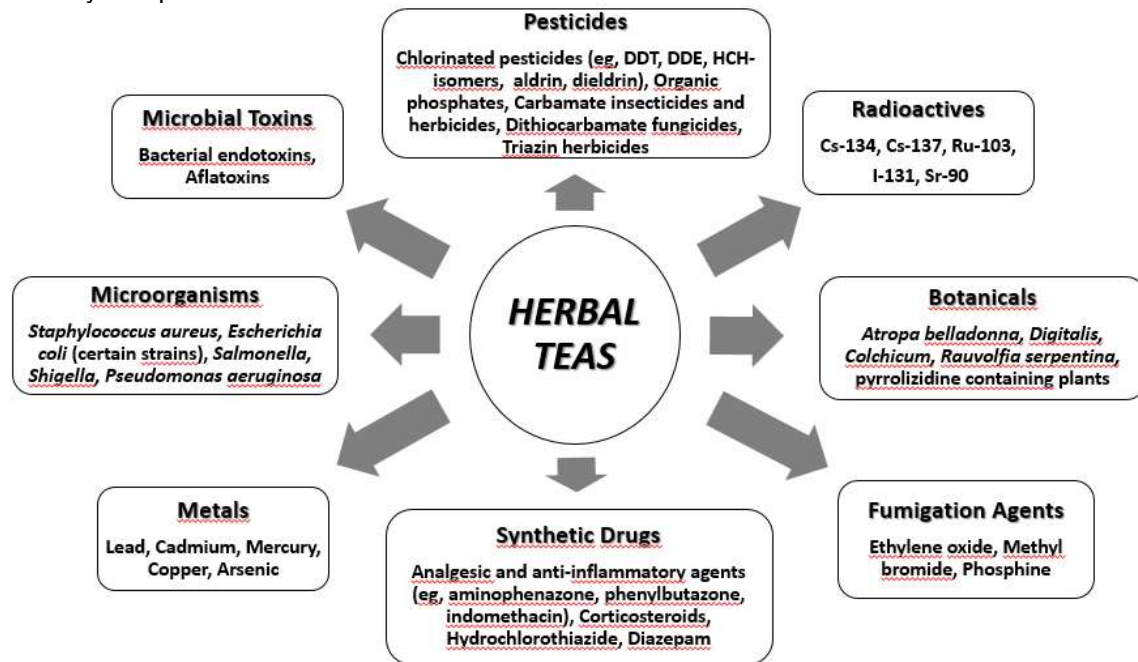


Figure 1: Herbal Teas exposed to several toxic contaminants

Herbal teas can be exposed to several toxic contaminants of different nature (Figure 1). In sum, we can categorise them into three categories: (1) contaminants linked to the plant, (2) contaminants that provide from environment and (3) contaminants due to humans.

Contaminants linked to the plant

Toxic contaminants related to the plant include toxic botanicals, microbial toxins, toxic metabolites or even living microbes such as bacteria, viruses, yeasts, parasites, insect larvae and eggs and other organisms (De Smet et al., 2004).

The misidentification of plants or the presence of undeclared species can cause serious problems. In certain case reports, the part of the plant used for the herbal product contains compounds like alkaloids of the cysteine type, which are known to be toxic. It is the case of *Sarothamni scoparii* flos that are provided from

Spartium junceum (Spanischer Ginster) rather than *Sarothamnus scoparius* (Besenginster) (de Smet et al., 1999). Also of interest, it was demonstrated that the use of contaminated roots by *Aristolochia frangchi*, in Chinese herbal teas, containing an important amount of aristolochic acid. This last one is known for its nephrotoxic properties and carcinogenic effects on rodents and humans (Wang et al., 2018; Krell, and Stebbing, 2013; Chen et al., 2012). The adulteration of plants with those containing acids can cause serious problems of human health.

Unlike to synthetic materials, the use of vegetables can be associated to microbial contamination and subsequent adverse effects. A recent study investigates the bacterial and fungal contamination of 26 herbal teas and revealed the presence of bacterial isolates like *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Serratia marcescens*, *Salmonella typhimurium*, *Pseudomonas*

fluorescens and *Escherichia coli*. Fungal isolates were *Aspergillus niger*, *Aspergillus flavus*, *Penicillium expansum*, *Rhizopus stolonifer* and *Fusarium solani*. This study also revealed that the highest occurrence contamination (100%) was attributed to *Bacillus subtilis* for bacteria and *Aspergillus niger* for fungi and the lowest one to *Salmonella typhimurium* (3%) and *Rhizopus stolonifera* (10%) (Omogbai and Ikenemomeh, 2013).

Viruses can surprisingly be the source of microbial contamination. Indeed, Japanese researchers reported the case of a man infected by hepatitis E virus after few days passed in China. The nucleotide sequencing suggests that his hepatitis E was caused by infection with the Chinese strain of the virus, via the CHM (Ishikawa et al., 1995). The plausibility of this hypothesis was verified since the victim confirms his trip in China four months prior to the onset of his symptoms. Independently to microorganism contamination, the quality control of herbal teas should take into account the eventual presence of microbial toxins like endotoxins and mycotoxins especially aflatoxin, for which several deleterious effects are known: mutagenic, carcinogenic, teratogenic, neurotoxic and nephrotoxic (Stević et al., 2012). The European Pharmacopeia has established a limit of 2 µg/ml as a limit value of aflatoxin 1 not to exceed for some medicinal herbs (Kosalec et al., 2009).

Contaminants that provide from environment

Many contaminants occur naturally in the ground and the atmosphere but the most problematic factors that provide from the environment are heavy metals and radioactivity. Despite of the existence of many radioactive sources, including radionuclides, radioactivity is not of a real concern (de Smet et al., 1999). Heavy metals represent a group of inorganic elements endowed of harmful risks. They are stable in the environment and can be found in particular high concentrations in some regions. Heavy metals include lead, cadmium, arsenic, chromium, copper, mercury and zinc. Some plants have the ability to fix and accumulate these metals and therefore, can be used as environmental contamination markers. Heavy metal pollution can have a natural origin and accumulate in the soil or result from the emission of industrial wastes like gasoline, mine tailing, paint...etc. (Nagajyoti et al., 2010; Wuana and Okieimen, 2011).

Accumulation of heavy metals cause

problems for all life forms (de Oliveira et al., 2018). High concentrations of this toxic substances in the human body induce deleterious ailments: skin diseases (Arsenic) (Tseng et al., 1968; Yeh et al., 1973; Schwartz, 1997), neurological disorders and kidney damage (Mercury) (Clarkson et al., 2003; Albers et al., 1988), gastrointestinal effects and anaemia (Zinc) (Broun et al., 1990; Plum, et al., 2010) brain neurotoxicity (Lead) (Marchetti, 2003), lung cancer, pulmonary oedema, respiratory distress, pneumonitis, bone disorder, liver and kidney damage (Cadmium) (Godt et al., 2006; Johri et al., 2010). Each metal is defined by its limit value. This one is determined by the world health organization and is of about 1 mg/kg Arsenic, 0.3 mg/kg for Cadmium and 10 mg/kg for Lead (World Health Organization, 1998).

Contaminants due to humans

Contamination of herbal teas can be of an anthropogenic origin. Human use pesticides and fumigation agents to control or eradicate pests. Pesticides are categorised according to their targets to insecticides, fungicides, nematocides, ascaricides, herbicides, molluscicides...etc. and to their chemical structures to organochlorine (dichlorodiphenyltrichloroethane, DDT), organophosphorus, nitrogen-containing pesticides...etc.) (Kosalec et al., 2009). As pesticides, fumigation agents including ethylene oxide, methyl bromide and phosphine are harmful for human health (Alavanja et al., 2004). Overexposure to these toxic substances can trigger to the apparition of symptoms of the nervous system like headache, dizziness, nausea...etc. (Abdollahi et al., 2004). The European Pharmacopoeia has tabulated general limits for pesticides and fumigation residues. Methods for determinate the presence of these compounds in herbal drugs are also set by some Pharmacopoeias (Association, 1996). It is important not to exceed these limits and respect the absence of unsafety levels of these toxic substances.

Also of a great interest and independently of the above-mentioned categories, animal substances represent potent contaminants of herbal products. Indeed, surprising compounds can be found in Chinese herbal teas. It is the case of thyroid hormones in herbal remedies with anti-diabetic effects, suspected presence of ass hide glue and even, toad venom rich in toxic steroids and toxins (de Smet et al., 1999).

The quality assurance evaluation should

warrant to the consumer a final product free from any inadvertent contaminant like microorganisms, toxins, heavy metals, pesticide residues...etc. because the efficacy and the reliability of herbal teas are closely related to their safety. Thus, it is important to specify constituents of herbal teas, which can be considered as markers to monitor the quality, by using analytical methods dedicated to this purpose.

Parameters and methods of herbal tea quality control

Quality control is based on four axes (Figure 2). It should investigate and have a regard on physical, chemical, botanical and biological aspects. Physico-chemical analysis covers the determination of ash remaining after ignition of herbal products, moisture content, solubility, viscosity, foreign matter, on one hand, and the estimation of heavy metal, pesticide residue and mycotoxin, mentioned above, on the other hand

(Choudhary et al., 2011). Botanical evaluation of herbal remedies includes both macroscopic and microscopic analysis, which requires the use of qualitative and quantitative techniques. However, due to the modern interest given to value-added products, macroscopic methods, based on sensory evaluation parameters (size, shape, odour, colour, taste and texture) and habitually used to detect adulteration or misnaming species become insufficient especially when the native plant structure is destroyed. The advent of chromatographic techniques has facilitate the identification of herbal teas constituents and helps to set quality standards. Also of interest is the study of biological and pharmacological parameters including pharmacokinetics, pharmacodynamics, stability, dosage, toxicity evaluation and chemical profiling of the herbal formulations (Choudhary et al., 2011).

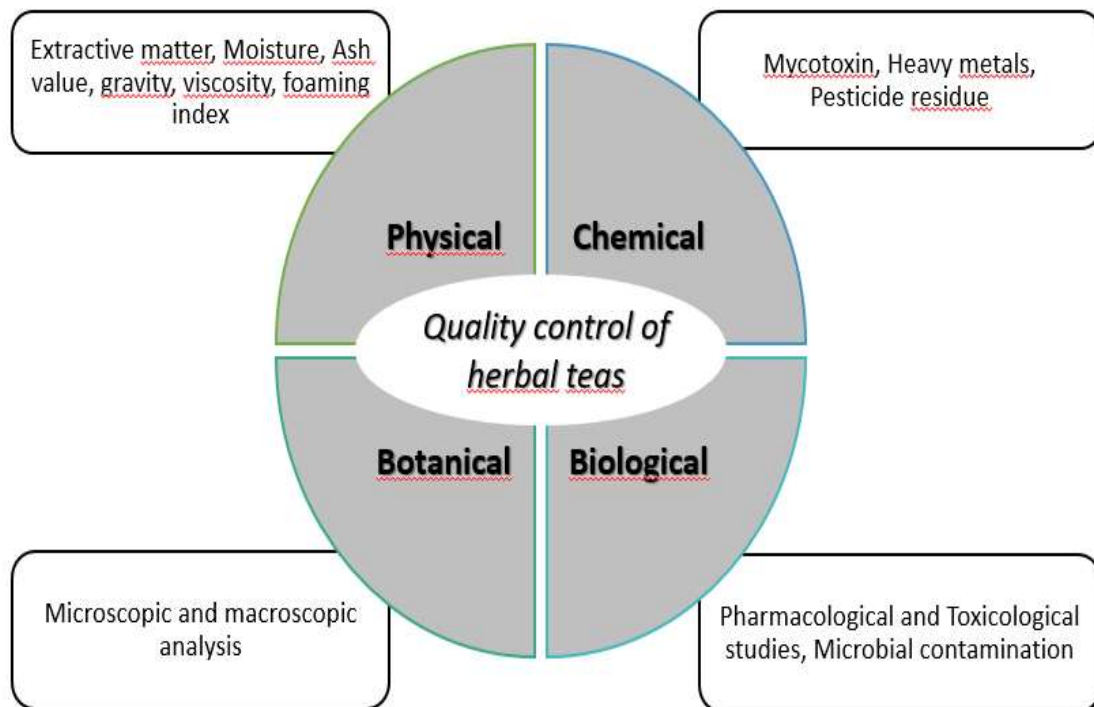


Figure 2: Quality control of herbal teas

Analytical techniques aim to quantify the amount of active substances and thus determine their biological effects on human health. Each technique used is defined by its strengths and weaknesses, so before any analyse, analyst should choose the most appropriate method among a large panel of those available. We shall summarize the most important of them and highlight on their characteristics.

Electrophoresis methods

Electrophoresis dates from the seventies. Used to isolate and identify several products including drugs, antibiotics, coumarins, alkaloids, flavonoids, Chinese herbal preparations...etc., this technique has rapidly proven its powerful separating capacity (Isaaq, 1999). The principle is based on the migration of particles, when an electric field is applied. Many variants of electrophoresis exist including gel electrophoresis, 2-D electrophoresis, isoelectric focusing, high-resolution electrophoresis, capillary electrophoresis (CE) and many others. However, CE is widely used in the quality control of herbal teas because of its rapidity, versatility and high separation efficiency. It needs only few amounts of reagents when compared to the most popular high performance liquid chromatography protocols and allows analysis of either small molecules of low molecular weight like drugs or macromolecules like nucleic acids and proteins. It can also be paired to chromatography and thus, allowing to confirm obtained results. However, enhancing the resolution of capillary electrophoresis has been detrimental to its reproducibility (Shulammithi et al., 2016). CE can address the numerous issues of food authenticity of health concern including beverages, fruit and vegetable, meals...etc. in order to avoid adulterations and ensure safety to consumers. Recently, many studies have been reported unravelling the use of such techniques in herbal tea remedies (Liu and Sheu, 1992; Başkan et al., 2007). As an example of application, the determination of flavonoid amounts and inorganic cations can be achieved using CE (Carducci et al., 2000; Chi et al., 2009).

Atomic absorption spectroscopy (AAS)

AAS is no longer restricted to the knowledge of some scientists, chemists or even astrophysicists, this technique has gained territory and is now extended to the medical and pharmaceutical fields. AAS is particularly convenient for the determination of heavy metals

in a large range of matrices including biological, environmental, clinical, geological samples and herbal drugs. This widely used technique allows detection of both trace ($\mu\text{g/mL}$) and ultra-trace ($\text{sub}\mu\text{g/mL}$) levels of metals (Venkateswarlu and Gouthami 2015). The principle is based on measurement of the absorbed radiation, when sample is excited by electromagnetic radiation. There are two variants of AAS: Flame atomic absorption spectroscopy (FAAS) and Electrothermal atomic absorption spectroscopy (ETAAS) depending on the source of atomization which can be flames or electrothermal atomizers, respectively (Smichowski and Londonio, 2018). AAS plays an important role in the analysis of herbal remedies, however, this method suffers from high detection limits ((Venkateswarlu and Gouthami 2015). In this field, AAS is especially used in quality control and several recent studies have used it for the evaluation of mineral or metal content in the herbal preparations including magnesium, calcium, sodium, cadmium, zinc, copper and others (Prkić et al., 2018; Afieroho et al., 2018; Al-Othman et al., 2012; Zhong et al., 2016; Kalny et al., 2007; Cabrera et al., 2003).

Gas chromatography (GC)

Nowadays, GC continues to prove its merit and eminence among other analytical techniques in the field of quality control. This technique responds to the principle of the redistribution of compounds present in a mixture, between a stationary phase which is a liquid, a solid or both and a mobile phase in the form of gas, this is why this technique is also called gas liquid chromatography (Shulammithi et al., 2016). Main advantages of this method are its high selectivity, sensitivity, resolution, good accuracy and precision. It can be also used for a wide dynamic concentration range (Santos and Galceran, 2002). However, the most serious disadvantage is its lack of suitability for thermo labile and non-volatile compounds (Shulammithi et al., 2016). GC can be coupled to other techniques like mass spectrometry and find applications, for instance, in determination of the presence of volatile pesticides residues in Chinese teas, by providing quantitative and qualitative information (Figure 3) (Huang et al., 2007; Lozano et al., 2012; Schurek et al., 2008).

<p style="text-align: center;">HPLC-UV Detector</p>	<ul style="list-style-type: none"> • Substances must be <u>chromophores</u> • UV detector not able to <u>detect all molecules in complex herbal teas</u> • Do not <u>detect contaminants such as heavy metals</u>
<p style="text-align: center;">LC-MS</p>	<ul style="list-style-type: none"> • Gives information on the structure of the <u>molecules of herbal teas</u> • The <u>number of molecules to be identified is higher than that of HPLC-UV</u> • Can <u>identify a wide variety of pesticides in herbal teas</u> • Limited to <u>detect volatile pesticides in herbal teas</u>
<p style="text-align: center;">GC-MS</p>	<ul style="list-style-type: none"> • Can <u>detect beneficial volatile molecules in herbal teas</u> • Can <u>detect toxic volatile molecules like cyanide present in some plants</u> • Can <u>detect volatile pesticides in herbal teas</u>

Figure 3: Qualitative and quantitative determination of herbal teas by using different analytical tools

Introduction of the two-dimensional GC in recent years allows overcoming problems encountered with the mono-dimensional GC related to the difficult separation of individual constituents of complex mixtures in some cases of phytochemical study especially that of herbal teas (Mondello et al., 2005). Bi-dimensional GC can, in turn, be coupled to a mass spectrometer, and when a high resolution time-of-flight (TOF) mass spectrometer is used, it gives rise to a powerful tool in the identification of bioactive compounds present in some medicinal plants (Cao et al., 2011). As an example of application, GC was used for the determination of a pool of flavonoids in *Krachaidum*, a Thai herb, despite of the similarity and polarity of these compounds in this herb. This study pointed out the efficiency and rapidity of GC compared to HPLC in determining and detecting flavonoids in a reasonable time (Sutthanut et al., 2007).

High-performance liquid chromatography (HPLC)

HPLC, also known as High Pressure Liquid Chromatography, is one of the most popular techniques defined by a wide spectrum of use including clinical chemistry, pharmaceutical industry, food and environmental analyses, synthetic chemistry...etc. (Olsen et al., 2006; Zotou et al., 2012). This analytical technique has gained its popularity because of its reliability, versatility, good repeatability, easiness to use and non-restriction to volatile samples (Shulammithi et al., 2016). HPLC is applied to all kinds of herbal

teas as it allows a good and reproducible separation of caffeine, catechins, theobromine, gallic acid and theophylline (Sharma et al., 2005). Some techniques have been optimized in order to gain in efficacy with a higher separation power like reversed-phase HPLC (RP-HPLC), which is the most one widely used in the analysis of herbal teas, micellar electro kinetic capillary chromatography (MECC), high speed counter current chromatography (HSCCC), strong anion exchange HPLC (SAX-HPLC) and low pressure size exclusion chromatography (SEC) (Shulammithi et al., 2016). However, simple HPLC is not able to provide qualitative information or structure elucidation and must be coupled to HPLC-Infra rouge, HPLC- Nuclear magnetic resonance and HPLC-Mass spectroscopy. Advances in HPLC offer a powerful tool for the investigation of quality control of herbal teas (Zimmermann et al., 2011). For instance, ultra HPLC (UHPLC), using sub-2 μm particle size column, allows analysis nine times faster than traditional HPLC even it is costly. The most common detection method used in HPLC analysis is single wavelength UV detector. However, due its inability to detect non-chromogenic compounds, mostly present in herbal remedies, another method is used in a recent decade, it is about the evaporative light scattering detection (ELSD), which is an excellent detection method convenient for chromogenic compounds (Shulammithi et al., 2016).

Liquid chromatography-mass spectrometry (LC-MS)

Thin-layer chromatography (TLC) is a method for the detection of fingerprint of plants. TLC is a simple and inexpensive method. However, the separation and detection of molecules by TLC are limited. LC-MS has become the preferred method for the analysis of multicomponents of herbal teas (Figure 3). For example, the tea *Psoralea corylifolia* is widely used in China for its anti-cancer, antioxidant and antibacterial properties. This herbal tea was analyzed by LC-MS which was able to identify the identity of several molecules of this herbal tea. Another example is the analysis of *multirrhiza salivvia*-based herbal tea by LC-MS, which revealed the presence of non-polar diterpenoids as they have beneficial effects on cardiovascular and cerebral diseases. The use of LC-MS has helped to prove the quality and effectiveness of herbal teas for the treatment of brain and cardiovascular diseases. For example, LC-MS revealed the presence of the stemona alkaloids of therapeutic interest in herbal teas based on *Sanicula tuberosa*. This alkaloid cannot be detected by HPLC-UV because it is not sensitive to direct UV detection due to the absence of UV absorbing chromophores. Another example is the herbal tea *Caulerpa racemosa* largely used in traditional medicine for the treatment of fever and insomnia. The analysis of this tea by the HPLC-UV is used to detect the presence of diterpenes glucosides however analysis by LC-MS is employed to reveal the presence of saponins in this tea. Another example is the Naodesheng tea which is indicated for the treatment of cerebral arteriosclerosis and ischemic stroke. The LC-MS analysis of this herbal tea revealed the presence of ten types of flavones and ginsenosides. These molecules are particularly discovered with the LC-MS. In addition, the recent use of LC-MS has allowed the quantification of molecules in complex herbal teas.

Biological analysis: *In vitro* and *in vivo* tests of herbal teas

Biological analysis tests of plants are various. There are studies that prefer *in vivo* testing while others support *in vitro* testing for plant analysis. For example, China has directly introduced traditional Chinese medicine knowledge in hospitals. Plants are selected on the basis of traditional medical practices and are introduced in hospitals for *in vivo* clinical evaluation (Chadwick et al., 2008). Therefore, the

in vitro studies are carried out in the research centers (chemical and toxicological) on the basis of clinical outcome. However, other researches prefer the way back. It begins with *in vitro* studies that consist of isolating bioactive molecules from plants without taking into consideration their traditional medicinal knowledge. These bioactive molecules isolated from plants are given to patients (Chadwick et al., 2008). These studies consider, in this case, that the plant is made up of a single bioactive molecule while it consists of thousands of different molecules. The plant is not a unique molecule but it works by mechanism of synergy between all molecules present in the mixture. Other studies prefer to use laboratory animals to test plant preparations from traditional Brazilian folk medicine (Chadwick et al., 2008). Based on the animal results they select plants that have more therapeutic effects and less risk of toxicity and introduces them into the health services. Some preparations of herbal teas appear to be inactive when used for *in vitro* tests such as the use of some solvent of extraction that can suppress the activity of the plant (Chadwick et al., 2008). However, the use of herbal teas by traditional medicine as a decoction protects the activity of the plant. These traditional medicine have experience directly on the human being and have tested through seals thousands of remedy (Chadwick et al., 2008). Other studies consider that *in vivo* testing of human is impossible to test toxic plants because the human body is not as strong as the body of animals. In addition, the exposure time in clinical trials of human volunteers is limited and prefers *in vitro* tests on isolated cells, tissues or enzyme receptors (Chadwick et al., 2008). However, according to these studies, it is limited to a single target whereas the herbal teas consist of plants that can have several targets when they entered the body. The results of *in vivo* clinical studies have helped to reveal the effects of medicinal plants on several diseases. On the other hand, they could not explain the mechanisms of action at the cellular and molecular level (Liu, 2011). Other studies have demonstrated differences between *in vivo* tests in animals and humans. For example, *Cryptolepis sanguinolenta* extracts are active against human infections while they are inactive against infections in animal. This shows that the human body's reaction to plants is not the same in animals. Same as the results of testing plants on animals are not always applicable in humans.

Commercial aspect

Preparation of commercial herbal mixtures

Commercial herbal teas are prepared either by street vendors or by individual traditional healers. They are often packaged in recycled bottles with handwritten labels. Other types of commercial herbal teas are manufactured in large quantities by professionals and private contractors in factories (Ndhlala et al., 2011). Despite the attempts to modernize and standardize commercial herbal teas, it still retains the social heritage of the people. For example, Ibhubezi tea is prepared in a large volume of water and patients must take a quarter of this tea to cure fungal or influenza infections (Ndhlala et al., 2011). Another example is kava tea which has long been marketed for its anti-anxiety effects while it is one of the commercial herbal teas that cause hepatitis. However, the same kava tea was prepared by traditional methods did not cause any cases of hepatitis. The methods of preparing herbal teas range from simple brewing processes to more complex procedures that use alcohol and other organic solvents to dissolve the essences of the plant. In some cases, the addition of drugs, such as aspirin, has been registered for certain types of herbal teas (Cano et al., 2004). Preparations of herbal teas used as sedatives mainly contain aromatic plant species, rich in active essential oils, which exert an antispasmodic, antibacterial and soothing effect for the stomach (Cano et al., 2004). The number of plants which enter into the preparation of herbal teas can increase their therapeutic effects as they may decrease like it is the case for the *Echinacea pupasea* herbal tea which has more effects when it is prepared alone. Other plants diminish their effectiveness (Hudson, 2016). Some methods of herbal tea preparation can influence the final concentration of their active substances. This is the case of glucofrangulin molecules that are not found in the herbal tea by simple infusion. To recover these molecules in the final concentration of the tea buckthorn bark, the method of preparation used is the decoction five minutes followed by two hours of infusion (Jean et al., 2008).

Therapeutic herbal tea market in Algeria

The consumption of herbal teas in Algeria is growing rapidly. Several import brands can be found in the market (Derouiche and Abdelnour, 2017). There are, for example, diet herbal tea "Dr. Ming's", "Sliming Herb", "Ritcher's", "Santé et

Vie", "Slimnat System", "Ali" and "FVR". There are other brands of herbal teas produced in Algeria such as "Imane with ginger and honey lemon" for intestinal gas. In the same range, there is "Imane ginger honey jujube" to treat cough, bronchitis, pneumonia, colds and hypotension. Other companies in Algeria produce cholesterol herbal tea for the treatment of cholesterol excess and the prevention of its high levels. There is also the karkade derived from *Hibiscus sabdariffa* which is used for reducing the risk of cardiovascular diseases. The existence of this type of herbal teas used for their action on the heart can lead to health risks for patients suffering of heart problems. These herbal teas are formulated by plants containing cardiotoxic components that can lead to cardiac arrest.

Another brand of herbal tea "Walada bébé", manufactured locally, has for action the stimulation of lactation. This herbal tea can be dangerous for the baby because it is not controlled and can contain unknown components that can pass to the baby through breast milk. There is also brands of herbal teas especially devoted to lose weight like: "Soltane rahat el bal", "Dr. Ming's", "Sliming Herb" and "Ritcher's". This herbal tea has the property of acting on the bladder to lose weight but by this action, dramatic risks leading to death can occur due to the loss of water resulting from the stimulation of the bladder. Another example of herbal teas in Algeria is the soothing baby tea number 8. This herbal tea facilitates the baby's sleep. It is constituted by the linden plant. Studies have shown that the linden inhibits lipase which increases the temperature of infants and prevents their growth (Chantre et al., 2002). Other studies have shown that lipid degradation by lipase inhibition leads to cancer development (Greenberg et al., 1992).

In Algeria, herbal teas market is growing significantly and is based mainly on imports. However, imports are not subject to control of plant performance, quality and toxicity. In addition, the trade of herbal teas in Algeria is not evolved around a structured legislative control. The pharmaceutical regulation covers both medicinal products for human and veterinary uses and includes a series of laws such as the order of June 25th, 2005 laying down the procedure and expertise of a pharmaceutical product subject to registration. There is also the law n° 85-05 of 26 Joumada El Oula 1405 corresponding to the February 16th, 1985 relating to the protection and the promotion of the health, modified and supplemented by the executive decree n° 92-284

of the bearing July 6th, 1992, relating to the registration pharmaceutical products for human use. Order n° 37 of August 23rd, 1998, laying down the procedures for analytical, pharmacotoxicological and clinical expertise applied to pharmaceutical products (Bouzabata et al., 2017). However, there is no specific regulation on herbal teas. The European legislation qualifies traditional medicines herbal products, whose use is at least thirty, including at least 15 years in the European Union, which are intended to be used without the supervision of a health professional and that are not administered by injection. Indeed, this procedure will provide the same guarantee as usual procedure. However, it will limit clinical studies that are not necessary for traditional herbal medicines. It has been stated that the decisive criterion for herbal products subjected to this type of simplified procedure is essentially based on traditional use or medicinal tradition, as evidenced by bibliographic elements or expert reports. The registration file includes information and documents from a pharmaceutical file, in particular those relating to quality, safety and efficacy. However, Algerian legislation imposes, on a mandatory basis and under the penalty of inadmissibility of registration files, clinical and pharmacotoxicological studies for plant based drug similar to all drugs, regardless to the age of traditional use. This registration procedure is cumbersome because of the cost of required tests and remains a handicap for a better development of herbal teas. Therefore, this regulation does not favor the control of herbal tea marketing in Algeria.

CONCLUSION

Herbal teas have accompanied man since the earliest times of his happiness and misfortune. Yerba mate was always a relaxing tea, a joy that unites families in Paraguay, for the pleasure it brings. The cola nut helps Africans fight poverty by giving them energy and strength. Herbal teas supported man to relieve the simplest symptoms up to serious illnesses. However, the use of herbal teas must be controlled, as their components may contain toxic elements that present a high risk for important functions. Today, the development of control methods makes it possible to detox elements. Unfortunately, many herbal teas are marketed without quality control. In Algeria, the use of herbal teas is increasing rapidly due to the presence on the market of several brands imported from abroad. They are sold without any control of their components. The

lack of control methods for herbal teas in Algeria can put the health of consumers at risk of disease progression. Herbal teas are beneficial to health if they are controlled and do not contain components that are toxic to the human body. For this reason, it is necessary to analyze herbal teas using control methods ensuring the distribution of herbal teas without danger to the consumer. We hope that this work will be very useful for the control of the market of Herbal teas in Algeria

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

ACKNOWLEDGEMENT

The authors would like to express their sincere thanks and gratitude to CRAPC, for providing the main sponsorship for this work. Authors would like also to thank Institute of Bio product Development (IBD) and Research Management Center at UTM, Malaysia, and also Global Agro Innovation (HK) Limited for partial support through grant No. R.J130000.7609.4C273.

AUTHOR CONTRIBUTIONS

LB, MMB, YB, AZB, AN, and BECHZ involved in data collection and writing of the manuscript. LB, MMB, KB, and HAE designed the work, DJD, TH, HAE reviewed the manuscript. All authors read and approved the final version.

Copyrights: © 2020@ author (s).

This is an open access article distributed under the terms of the [Creative Commons Attribution License \(CC BY 4.0\)](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

REFERENCES

- Abdollahi M, Ranjbar A, Shadnia S, Nikfar S and Rezaie A, 2004. Pesticides and oxidative stress: a review. *Med Sci Monitor* 10(6):RA141-147.
- Afierohe OE, Achara F, Adewoyin B and Abo KA, 2018. Determination of cadmium, chromium and lead in four brands of herbal bitters preparation sold in Benin-city, Southern Nigeria. *Afric J Environ Sci and Technol*

- 12(5): 186-190.
- Agouillal F, Moghrani H, Nasrallah N, Hanapi Z, Taher Z and El-Enshasy HA, 2018. Coupling ultrasound with enzyme-assisted extraction of essential oil from Algerian *Artemisia herba-alba* Asso. J Sci Ind Res 77: 465-471.
- Aladdin A, Ata R, Pareek A, Othman NZ, Abd Malek R and El Enshasy H, 2017. Biotechnological aspects and pharmaceutical applications of bacterial proteases. Der Pharmacia Lett 9(2): 9-20.
- Alavanja MC, Hoppin JA and F. Kamel F, 2004. Health effects of chronic pesticide exposure: cancer and neurotoxicity. Annu. Rev. Public Health 25: 155-197.
- Albers JW, Kallenbach LR, Fine LJ, Langolf GD, Wolfe RA, Donofrio PD, Alessi AG, Stolp-Smith KA and Bromberg MB, 1988. Neurological abnormalities associated with remote occupational elemental mercury exposure. Ann Neurol 24(5): 651-659.
- Alolga RN, Gan Y, Zhang G, Li J, Zhao Y-J, Kakila JL, Chen Y, Li P and Qi L-W, 2015. Pharmacokinetics of a multicomponent herbal preparation in healthy Chinese and African volunteers. Sci Rep 5: 12961.
- Al-Othman ZA, Yilmaz E, Sumavli HM and Soylak M, 2012. Evaluation of trace metals in tea samples from Jeddah and Jazan, Saudi Arabia by atomic absorption spectrometry. Bull Environm Contam Toxicol 89(6): 1216-1219.
- Arora E, Khajuria V, Tandon VR, Sharma A, Mahajan A, Gillani ZH and Choudhary N, 2015. To evaluate efficacy and safety of *Caralluma fimbriata* in overweight and obese patients: A randomized, single blinded, placebo control trial. Perspect Clin Res 6(1): 39-44.
- Association, B.H.M., British herbal pharmacopoeia 1996. Bournemouth: British Herbal Medicine Association 212p. ISBN, 1996. 903032104.
- Başkan S, Öztekin N and Erim FB, 2007. Determination of carnosic acid and rosmarinic acid in sage by capillary electrophoresis. Food Chem 101(4): 1748-1752.
- Blömeke B, Poginsky B, Schmutte C, Marquardt H and Westendorf J, 1992. Formation of genotoxic metabolites from anthraquinone glycosides, present in *Rubia tinctorum* L. Mutat Res 265(2): 263-272.
- Bouzabata A, 2017. Les médicaments à base de plantes en Algérie: réglementation et enregistrement. Phytothérapie, 15(6): 401-408.
- Brito FA, Lima LA, Ramos MF, Nakamura MJ, Cavalher-Machado SC, Siani AC, Henriques MG and Sampaio AL, 2007. Pharmacological study of anti-allergic activity of *Syzygium cumini* (L.) Skeels. Braz J Med Biol Res 40: 105-115.
- Broun ER, Greist A, Tricot G and Hoffman R, 1990. Excessive zinc ingestion: a reversible cause of sideroblastic anemia and bone marrow depression. JAMA 264(11): 1441-1443.
- Cai R. and Guo Y, 1974. Report of 24 cases with intoxication of *Tripterygium wilfordii* Hook F. Yi Xue Zi Liao, 1974. 1: 15.
- Cabrera C, Giménez R and López MC, 2003. Determination of tea components with antioxidant activity. J Agric Food Chem 51(15): 4427-4435.
- Campos dOMP, Riechelmann R, Martins LC, Hasan BJ, Casa FB and Del Giglio A, 2011. Guarana (*Paullinia cupana*) Improves fatigue in breast cancer patients undergoing systemic chemotherapy. J Alt Complement Med 17(6): 505-512.
- Cano JH and Volpato G, 2004. Herbal mixtures in the traditional medicine of Eastern Cuba. J Ethnopharmacol 90(2): 293-316.
- Gao G, Shan Q, Li X, Cong X, Zhang Y, Cai H and Cai B, 2011. Analysis of fresh *Mentha haplocalyx* volatile components by comprehensive two-dimensional gas chromatography and high-resolution time-of-flight mass spectrometry. Analyst 136(22): 4653-4661.
- Carducci CN, Dabas PC and Muse JO, 2000. Determination of inorganic cations by capillary ion electrophoresis in *Ilex paraguariensis* (St. H.), a plant used to prepare tea in South America. J AOAC Int 83(5): 1167-1173.
- Chadwick DJ and Marsh J, 2018. Ethnobotany and the search for new drugs. Vol. 185. John Wiley & Sons.
- Chantre P and Lairon D, 2002. Recent findings of green tea extract AR25 (Exolise) and its activity for the treatment of obesity. Phytomed 9(1): 3-8.
- Chen CH, Dickman KG, Moriya M, Zavadil J, Sidorenko VS, Edwards KL, Gnatenko DV, Wu L, Turesky RJ, WU XR, Pu YS and Grollman AP, 2012. Aristolochic acid-associated urothelial cancer in Taiwan. Proc Nat Acad Sci USA 109(21): 8241-8246.
- Chen Z, Gu K, Zheng Y, Zheng W, Lu W and Shu

- XO, 2008. The use of complementary and alternative medicine among Chinese women with breast cancer. *J Altern complement Med* 14(8): 1049-1055.
- Chi L, Li Z, Dong S, He P, Wang Q and Fang Y, 2009. Simultaneous determination of flavonoids and phenolic acids in Chinese herbal tea by beta-cyclodextrin based capillary zone electrophoresis. *Microchimica Acta* 167(3-4): 179-185.
- Chopra I, Shales S and Ball P, 1982. Tetracycline resistance determinants from groups A to D vary in their ability to confer decreased accumulation of tetracycline derivatives by *Escherichia coli*. *Microbiology* 128(4): 689-692.
- Choudhary N and Sekhon BS, 2011. An overview of advances in the standardization of herbal drugs. *J Pharmaceut Edu Res* 2(2): 55-70.
- Ciociu M, Mirón A, Mares L, Tutunaru D, Pohaci C, Groza M and Badescu M, 2009. The effects of *Sambucus nigra* polyphenols on oxidative stress and metabolic disorders in experimental diabetes mellitus. *J Physiol Biochem* 65(3): 297-304.
- Clarkson TW, Magos L and Myers GJ, 2003. The toxicology of mercury—current exposures and clinical manifestations. *New England J Med* 349(18): 1731-1737.
- De Andrade CG, Mesquita LMdS, Murador DC, Bragab ARC, Rosso VVd, Almeida OJG and Vilegas W, 2018. Application of electrospray ionization mass spectrometry fingerprinting associated with macroscopic and histological analysis for *Plantago major* herbal infusions quality control. *Food Res Int* 107: 314-324.
- Deng G. and Cassileth B, 2013. Complementary or alternative medicine in cancer care—myths and realities. *Nat Rev Clin Oncol* 10: 656-664.
- Derouiche MT and Abdennour S, 2017. Enquête sur la qualité des tisanes médicales en Algérie. *Nut Clin et Métabol*, 31(1): 77-78.
- de Smet, PA, 1999. Overview of herbal quality control. *Drug Inform J* 33(3): 717-724.
- De Smet PA, 2004. Health risks of herbal remedies: an update. *Clin Pharmacol Therap* 76(1): 1-17.
- De Oliveira LM, Das S, da Silva EB, Gao P, Gress J, Liu Y and Ma LQ, 2018. Metal concentrations in traditional and herbal teas and their potential risks to human health. *Sci Total Environ* 633: 649-657.
- Eldalo AS, Alotaibi MN, Alenazi TO, Albogami HA and Mohamed KM, 2017. Use of herbal medicines in the treatment of obesity in Taif, Saudi Arabia. *Saudi J Med Medical Sci* 5(2): 149-154.
- El Deeb N, El-Adawi H, Sharaf M and El Enshasy HA, 2018. Targeting pro-inflammatory cytokines and chemokine as potential novel strategy in adjuvant development for anti-HCV therapy. *J Sci Ind Res* 77: 510-515.
- Fan X, 1993. Inhibitory effect of antitumor-B and retinamide on precancerous lesions of the bladder in rats). *Zhongguo yi xue ke xue yuan xue bao. Acta Acad Med Sin* 15(1): 71-73.
- Gershwin ME and A. Belay, 2007. *Spirulina in human nutrition and health*. 2007: CRC press.
- Godt J, Scheidig F, Siestrup CG, Esche V, Brandenburg P, Reich A and Groneber DA, 2006. The toxicity of cadmium and resulting hazards for human health. *J Occup Med Toxicol* 1(1): 22.
- Goldstein JA and de Morais SM, 1994. Biochemistry and molecular biology of the human CYP2C subfamily. *Pharmacogen*, 4(6): 285-299.
- Gomaa SE, Yahayu M, Nuriyadi M, Dailin DJ and El Enshasy H, 2019. Antimicrobial compounds from *Catharanthus roseus*-A Review. *International J Sci Technol Res* 8:113-121.
- Gonzalez de Mejia, E., Song YS, Ramirez-Mares MV, Kobayashi H, 2005. Effect of yerba mate (*Ilex paraguariensis*) tea on topoisomerase inhibition and oral carcinoma cell proliferation. *J Agric Food Chem* 53(6): 1966-1973.
- Greenberg AS, Nordan RP, McIntosh J, Calvo JC, Scow RO, Jablons D, 1992. Interleukin 6 reduces lipoprotein lipase activity in adipose tissue of mice in vivo and in 3T3-L1 adipocytes: a possible role for interleukin 6 in cancer cachexia. *Cancer Res* 52(15): 4113-4116.
- Guérin-Méneville FÉ and de Sainson M, *Dictionnaire pittoresque d'histoire naturelle et des phénomènes de la nature*. 1837: Au Bureau de souscription.
- Gui QF, Xu ZR, Xu KY, Yang YM, 2016. The efficacy of Ginseng-related therapies in type 2 diabetes mellitus: An updated systematic review and meta-analysis. *Medicine* 95(6): e2584-e2584.
- Hamidpour M, Hamidpour R, Hamidpour S and Shahlari M, 2014. Chemistry, pharmacology, and medicinal property of sage (*salvia*) to

- prevent and cure illnesses such as obesity, diabetes, depression, dementia, lupus, autism, heart disease, and cancer. *J Trad Complement Med* 4(2): 82-88.
- Hamilton RJ, 2009. *Tarascon Pharmacopoeia* Jones & Bartlett Learning.
- Hajhashemi V and Klooshani V, 2013. Antinociceptive and anti-inflammatory effects of *Urtica dioica* leaf extract in animal models. *Avicenna J Phytomed* 3(2): 193-200.
- He RR, Chen L, Lin BH, Matsui Y, Yao XS, Kurihara H, 2009. Beneficial effects of oolong tea consumption on diet-induced overweight and obese subjects. *Chin J Integr Med* 15(1): 34-41.
- He SM, Li GG, Liu JP, Chan E, Duan W, Zhou SF, 2010. Disposition pathways and pharmacokinetics of herbal medicines in humans. *Curr Med Chem* 17(33): 4072-4113.
- Heck CI and De Mejia EG, 2007. *Yerba Mate Tea (Ilex paraguariensis): A comprehensive review on chemistry, health implications, and technological considerations.* *J Food Sci* 72(9): p. R138-R151.
- Heikens J, Fliers E, Endert E, Ackermans M and van Montfrans G, 1995. Liquorice-induced hypertension—a new understanding of an old disease: case report and brief review. *Neth J Med* 1995. 47(5): 230-234.
- Hong CT, Huang JK, Wang HY, Huang CC and Chen FA, 2014. Antioxidant and antifatigue activities of *Polygonatum alveolatum* Hayata rhizomes in rats. *Nutrients* 6(11): 5327-5337.
- Huang Z, Li Y, Chen B and Yao S, 2007. Simultaneous determination of 102 pesticide residues in Chinese teas by gas chromatography–mass spectrometry. *J Chromatogram B Anal Technol Biomed Life Sci* 853(1-2): 154-162.
- Hudson JB, 2016. *The Echinacea Herb Story: Tradition Meets Modern Science.* 2016: Friesen Press.
- Ihme N, Kiesewetter H, Jung F, Hoffmann KH, Birk A, Müller and Grützner KI, 1996. Leg oedema protection from a buckwheat herb tea in patients with chronic venous insufficiency: a single-centre, randomised, double-blind, placebo-controlled clinical trial. *Eur J Clin Pharmacol* 50(6): 443-447.
- Ishikawa K, Matsui K, Madarame T, Sato S, Oikawa K and Uchida T, 1995. Hepatitis E probably contracted via a Chinese herbal medicine, demonstrated by nucleotide sequencing. *J Gastroenterol* 30(4): 534-538.
- Iwamura C, Shinoda K, Yoshimura M, Watanabe Y, Obata Z and Nakayama T, 2010. Naringenin Chalcone suppresses allergic asthma by inhibiting the type-2 function of CD4 T cells. *Allergol Int* 59(1): 67-73.
- Jäger S, Beffert M, Hoppe K, Nadberezny D, Frank B and Scheffler A, 2011. Preparation of herbal tea as infusion or by maceration at room temperature using mistletoe tea as an example. *Sci Pharm* 79(1): 145-156.
- Jan M, 2014. Effects of *Ammi visnaga* (Bisnaga) extract on the volume and acidity of stimulated gastric secretion in fasting rabbits. *J Coll Phys Surg Pakistan* 24(1): 39-42.
- Jean B, 2008. *Pharmacognosy, Phytochemistry, Medicinal Plants (2 ed.-retirage broch").* Lavoisier.
- Jian Y. and Zhou S, 1987. Acute intoxication complicated with kidney damage. *Chin J Kidney Dis*, 13: 667.
- Johri N, Jacquillet G and R. Unwin, Heavy metal poisoning: the effects of cadmium on the kidney. *Biometals*, 2010. 23(5): 783-792.
- Joubert E, Gelderblom WC, Louw A and de Beer D, 2008. South African herbal teas: *Aspalathus linearis*, *Cyclopia* spp. and *Athrixia phyllicoides*-A review. *J Ethnopharmacol* 119(3): 376-412.
- Kalny P, Fijalek Z, Daszczuk A and Ostapczuk P, 2007. Determination of selected microelements in polish herbs and their infusions. *Sci Total Environ* 381(1-3): 99-104.
- Kane JA, Kane SP and S. Jain 1995. Hepatitis induced by traditional Chinese herbs; possible toxic components. *Gut*, 36(1): 146-147.
- KC VB and Krishnakumari S, 2006. *Cardiospermum halicacabum* suppresses the production of TNF-alpha and nitric oxide by human peripheral blood mononuclear cells. *Afric J Biomed Res* 9(2): 95-99.
- Khodadadi S, 2015. Role of herbal medicine in boosting immune system. *Immunopathol Pers* 1(1): e01-2.
- Kitagawa H, Munekage M, Ichikawa K, Fukudome I, Munekage E, Takezaki Y, Matsumoto T, Igarashi Y, Hanyu H and Hanazaki K, 2015. Pharmacokinetics of active components of Yokukansan, a traditional Japanese herbal medicine after a single oral administration to healthy Japanese volunteers: A cross-over, randomized study. *PLOS ONE* 10(7): e0131165.
- Kosalec I, Cvek J and Tomić S, 2009. Contaminants of medicinal herbs and herbal

- products. Arhiv za higijenu rada i toksikologiju, 60(4): 485-500.
- Krell D. and Stebbing J, 2013, Aristolochia: the malignant truth. The Lancet Oncol, 14(1): 25-26.
- Lam J and Wrang P, 1975. Flavonoids and polyacetylenes in *Dahlia tenuicaulis*. Phytochem, 1975. 14(7): p. 1621-1623.
- Lavergne R, 1989. Plantes médicinales indigènes: tisane et tisaneurs de la Réunion. Université Montpellier II-Sciences et Techniques du Languedoc.
- Lee CS, Kim YJ, Lee MS and Lee SJ, 2008. 18 β -Glycyrrhetic acid induces apoptotic cell death in SiHa cells and exhibits a synergistic effect against antibiotic anti-cancer drug toxicity. Life Sci 83(13): 481-489.
- Lemli J, Cuveele J and Verhaeren E, 1983. Chemical Identification of Alexandrian and Tinnevely Senna. Planta Med 49. 1983. 36-37.
- Li X, 2002. Chinese materia medica: combinations and applications. Elsevier Health Sciences.
- Lim TK, 2014. Edible Medicinal and Non Medicinal Plants: Vol 8, Flowers. Springer Netherlands.
- Ling S, Nheu L, Dai A, Guo Z and Komesaroff P, 2008. Effects of four medicinal herbs on human vascular endothelial cells in culture. Int J Cardiol 128(3): 350-358.
- Liu WJH, 2011. Traditional herbal medicine research methods: identification, analysis, bioassay, and pharmaceutical and clinical studies. John Wiley & Sons.
- Liu Y-M and Sheu S-J, 1992. Determination of quaternary alkaloids from *Coptidis rhizoma* by capillary electrophoresis. J Chromatogr A 623(1): 196-199.
- Lozano A, Rajski L, Belmonte-Valles N, Ucles A, Ucles S, Mezcuca M and Fernandez-Alba AR, 2012. Pesticide analysis in teas and chamomile by liquid chromatography and gas chromatography tandem mass spectrometry using a modified QuEChERS method: validation and pilot survey in real samples. J Chromatogr A 1268: p. 109-122.
- Malek K, Norazan M, Ramaness P, Othman NZ, Abd Malek R, Aziz R, Aladdin A and El Enshasy H, 2016. Cysteine proteases from *Carica papaya*: An important enzyme group of many industrial applications. IOSR J Pharm Biol Sci 11(2): 11-16.
- Marchetti C, 2003. Molecular targets of lead in brain neurotoxicity. Neurotoxicol Res 5(3): 221-235.
- Mattocks A, 1980. Toxic pyrrolizidine alkaloids in comfrey. The Lancet 316(8204): 1136-1137.
- Mohamad MF, Dailin DJ, Gomaa SE, Nurjayadi M and El Enshasy H, 2019. Natural colorant for food: A healthy alternative. Int J Sci Technol Res 8:3161-3166.
- Mondello L, Casilli A, Tranchida PQ, Dugo P and Dugo G, 2005. Comprehensive two-dimensional GC for the analysis of citrus essential oils. Flav Frag J F20(2): 136-140.
- Muramatsu T, Takagi K, Yashiki A, Sakurai S, Honoki K and Shirai T, 1995. Mucinous carcinoma of the skin. British J Dermatol 133(5): 820-821.
- Nagajyoti P, Lee K and Sreekanth T, 2010. Heavy metals, occurrence and toxicity for plants: a review. Environ Chem Lett 8(3): 199-216.
- Ndhala AR, Stafford GI, Finnie JF, Van Staden J, 2011. Commercial herbal preparations in KwaZulu-Natal, South Africa: The urban face of traditional medicine. South Afr J Bot 77(4): 830-843.
- Olsen BA, Castle BC and Myers DP, 2006. Advances in HPLC technology for the determination of drug impurities. Trends Anal Chem 25(8): 796-805.
- Omar HR, Komarova I, El-Ghonemi M, Fathy A, Rashad R, Abdelmalek HD, Yerramadha MR, Ali Y, Helal E and Camporesi EM, 2012. Licorice abuse: time to send a warning message. Ther Adv Endocrinol Metab 3(4): 125-138.
- Omogbai BA and Ikenebomeh M, 2013. Microbiological characteristics and phytochemical screening of some herbal teas in Nigeria. Eur Sci J 9(18) 149-160.
- Pan J, Zhang Q, Li K, Liu Q, Wang Y and You M, 2013. Chemoprevention of lung squamous cell Carcinoma by Ginseng. Cancer Prev Res 6(6): 530-539.
- Park S-J, Bae Y-C, Choi N-R, Ryu S-Y, Kwon Y-M and Joo J-C, 2014. Clinical study on constitutional herbal tea for treating chronic fatigue. J pharmacopuncture 17(4): 55-60.
- Plum LM, Rink L and Haase H, 2010. The essential toxin: impact of zinc on human health. International J Environ Res and Pub Health 7(4): 1342-1365.
- Prchalová J, Kovařík F and Rajchl A, 2017. Evaluation of the quality of herbal teas by DART/TOF-MS. J Mass Spectrom 52(2): 116-126.
- Prkić A, Politeo N, Giljanović J, Sokol V, Bošković P, Brkljača M and Stipišić A, 2018. Survey of content of cadmium, calcium, chromium,

- copper, iron, lead, magnesium, manganese, mercury, sodium and zinc in chamomile and green tea leaves by electrothermal or flame atomizer atomic absorption spectrometry. *Open Chem* 16: 228-237.
- Rabiei Z, Rafieian-Kopael M, Mokhtari S and Shahrani M, 2014. Effect of dietary ethanolic extract of *Lavandula officinalis* on serum lipids profile in rats. *Iranian J Pharm Res* 13(4): 1295-1301.
- Reddy BA, 2010. Digitalis therapy in patients with congestive heart failure. *Int J Pharm Sci Rev and Res*. 3(2): 90-95.
- Ridker PM, 1987. Toxic effects of herbal teas. *Arch Environ Health*. 42(3): 133-136.
- Salvador AC, Krol E, Lemos VC, Santos SAO, Bento FPMS, Costa CP, Almeida A, Szczepankiewicz D, Kulczynski B, Krejpacio Z, Silvestre AJD and Rocha S, 2017. Effect of elderberry (*Sambucus nigra* L.) extract supplementation in STZ-induced diabetic rats fed with a high-fat diet. *Int J Mol Sci* 18(1): 13.
- Sandoval M, Okuhama NN, Zhang XJ, Condezo LA, Lao J, Angeles FM, Musah RA, Bobrowski P and Miller MJ, 2002. Anti-inflammatory and antioxidant activities of cat's claw (*Uncaria tomentosa* and *Uncaria guianensis*) are independent of their alkaloid content. *Phytomed* 9(4): 325-337.
- Sang S, Lambert JD, Ho CT and Yang CS, 2011. The chemistry and biotransformation of tea constituents. *Pharmacol Res* 64(2): 87-99.
- Santos F and Galceran M, 2002. The application of gas chromatography to environmental analysis. *Trends Anal Chem* 21(9-10): 672-685.
- Sarmidi MR and El Enshasy H, 2012. Biotechnology for wellness industry: Concepts and biofactories. *Int J Biotechnol Well Ind* 1: 3-28.
- Schoental R, 1982. Health hazards of pyrrolizidine alkaloids: A short review. *Toxicol Lett* 10(4): 323-326.
- Schurek J, Portoles T, Hajslova J, Riddellova K and Hernandez F, 2008. Application of head-space solid-phase microextraction coupled to comprehensive two-dimensional gas chromatography-time-of-flight mass spectrometry for the determination of multiple pesticide residues in tea samples. *Anal Chim Acta* 611(2): 163-172.
- Schwartz RA, 1997. Arsenic and the skin. *Int J Dermatol* 36(4): 241-250.
- Singh B, Mishra A and Goel RK, 2011. Anticonvulsant activity of *Passiflora incarnata*: No role of chrysin. *J of Pharm Neg Res* 2011. 2(2): 51.
- Sharma V, Gulati A, Ravindranath S and Kumar V, 2005. A simple and convenient method for analysis of tea biochemicals by reverse phase HPLC. *J Food Compos and Anal* 18(6): 583-594.
- Shulammithi R, Shearanya M, Tejaswini R and Kiranmai M, 2016. Standardization and quality evaluation of herbal drugs. *IOSR J Pharm Biol Sci* 11(5): 89-100.
- Smichowski P and Londonio A, 2010. The role of analytical techniques in the determination of metals and metalloids in dietary supplements: A review. *Microchem J* 136: 113-120.
- Sofowora A., E. Ogunbodede E and Onayade A, 2013. The role and place of medicinal plants in the strategies for disease prevention. *Afr J Trad Compl and Altern Med* 10(5): 210-229.
- Stević T, Pavlovic S, Stankovic S and Savikin K, 2012. Pathogenic microorganisms of medicinal herbal drugs. *Arch Biol Sci* 64(1): 49-58.
- Stickel F, Baumüller HM, Seitz K, Vasilakis D, Seitz G, Seitz HK and Schuppan D, 2003. Hepatitis induced by Kava (*Piper methysticum rhizoma*). *J Hepatol* 39(1): 62-67.
- Sutthanut K, Sripanidkulchai B, Yenjai C and Jay M, 2007. Simultaneous identification and quantitation of 11 flavonoid constituents in *Kaempferia parviflora* by gas chromatography. *J Chromatogr A* 1143(1-2): 227-233.
- Tao X, Younger J, Fan FZ, Wang B and Lipsky PE, 2002. Benefit of an extract of *Tripterygium Wilfordii* Hook F in patients with rheumatoid arthritis: A double-blind, placebo-controlled study. *Arthritis Rheum* 46(7): 1735-1743.
- Tian J, Li M, Liao J, Li J and Tong X, 2013. Chinese herbal medicine Banxiaxixin decoction treating diabetic gastroparesis: A systematic review of randomized controlled trials. *Evid Based Evidence-Based Complement Alternat Med* 2013: 749495
- Tseng WP, Chu HM, How SW, Fong JM, Lin CS and Yeh S, 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. *J Natl Cancer Inst* 40(3): 453-463.
- van der Bijl P and van der Bijl P, 2012. Cardiotoxicity of plants in South Africa. *Cadiovasc J Afr* 23(9): 476-477.

- Vasanthi H. and Parameswari RP, 2010. Indian spices for healthy heart-an overview. *Curr Cardiol Rev* 6(4): 274-279.
- Vanderperren B, Rizzo M, Angenot L, Haufroid V, Jadoul M and Hantson P, 2005. Acute liver failure with renal impairment related to the abuse of Senna anthraquinone glycosides. *Ann Pharmacother* 39(7-8): 1353-1357.
- Venkateswarlu P and Gouthami B, 2015. An overview of recent applications of atomic absorption spectroscopy in determination of inorganic impurities in drugs and, plants and its extracts. *Int J Basic Appl Sci* 1(2): 37-45.
- Wang B-Q, 2010. *Salvia miltiorrhiza*: Chemical and pharmacological review of a medicinal plant. *J Med Plant Res* 4(25): 2813-2820.
- Wang L, Ding X, Li C, Zhao Y, Yu C, Yi Y, Zhang Y, Gao Y, Pan C, Liu S, Han J, Tian J, Liu J, Deng N, Li G and Liang A, 2018. Oral administration of *Aristolochia manshuriensis* Kom in rats induces tumors in multiple organs. *J Ethnopharmacol* 225: 81-89.
- Wang Y, Zhang Z, Kastens E, Lubet RA and You M, 2003. Mice with alterations in both p53 and Ink4a/Arf display a striking increase in lung tumor multiplicity and progression: differential chemopreventive effect of budesonide in wild-type and mutant A/J Mice. *Cancer Res* 63(15): 4389-4395.
- Wang Y, Zhang Z, Garbow JR, Rowland DJ, Lubet RA, Sit D, Law F and You M, 2009. Chemoprevention of lung squamous cell Carcinoma in mice by a mixture of Chinese herbs. *Cancer Prev Res* 2(7): 634-640.
- Wang Y, Yao R, Gao S, Wen W, Du Y, Szabo E, Hu M, Lubet RA and You M, 2013. Chemopreventive effect of a mixture of Chinese Herbs (antitumor B) on chemically induced oral carcinogenesis. *Mol Carcinogen* 52(1): 49-56.
- Wang Z, Li J, Ji Y, An P, Zhang S and Li Z, 2013. Traditional herbal medicine: A review of potential of inhibitory hepatocellular Carcinoma in basic research and clinical trial. *Evid Based Compl Alternat Med* 2013.268963.
- Wang ZY, Huang MT, Ho CT, Chang R, Ma W, Ferraro T, Reuhl KR, Yang CS and Conney AH, 1992. Inhibitory effect of green tea on the growth of established Skin papillomas in mice. *Cancer Res* 52(23): 6657-6665.
- Wang ZY, Hong JY, Huang MT, Reuhl KR, Conney AH and Yang CS, 1992. Inhibition of N-nitrosodiethylamine- and 4-(methylnitro samino)-1-(3-pyridyl)-1-butanone-induced tumorigenesis in A/J mice by green tea and black tea. *Cancer Res* 52(7): 1943-1947.
- Wirngo FE, Lambert MN, and Jeppesen PB, 2016. The Physiological Effects of Dandelion (*Taraxacum officinale*) in Type 2 Diabetes. *Rev Diabet Stud* 13(2-3): 113-131.
- Wong KY, Tan EY, Chen JJ, Teo C and Chan PM, 2014. The use of traditional Chinese medicine among breast cancer patients: implications for the clinician. *Ann Acad Med Singapore* 43(2): 74-78.
- Wong LYE, Leung PC, Tang J-L and Mercer SW, 2010. Use of dietary supplements by breast cancer patients undergoing conventional cancer treatment. *Patient Preference Adherence* 4: 407-414.
- World Health Organization, Quality control methods for medicinal plant materials. 1998. <https://apps.who.int/iris/handle/10665/41986>
- Wuana, RA and Okieimen FE, 2011. Heavy metals in contaminated soils: a review of sources, chemistry, risks and best available strategies for remediation. *Int Scholarly Res Notices*. 2013, article ID 402647.
- Xie W, Gu D, Li J, Cui K and Zhang Y, 2011. Effects and action mechanisms of Berberine and *Rhizoma coptidis* on gut microbes and obesity in high-fat diet-fed C57BL/6J mice. *PLOS ONE*, 2011. 6(9): e24520
- Yan Y, Wang Y, Tan Q, Hara Y, Yun TK, Lubet RA, You M, 2006. Efficacy of polyphenon E, red ginseng, and Rapamycin on benzo(a)pyrene-induced lung tumorigenesis in A/J Mice. *Neoplasia* 8(1): 52-58.
- Yeh S, 1973. Skin cancer in chronic arsenicism. *Human Pathol* 1973. 4(4): 469-485.
- Yong JWH, Ge L, Ng YF and Tan SN, 2009. The chemical composition and biological properties of coconut (*Cocos nucifera* L.) Water. *Molecules* 14(12): 5144-5164.
- Yun TK, Yun YS, and Han IW, 1983. Anticarcinogenic effect of long-term oral administration of red ginseng on newborn mice exposed to various chemical carcinogens. *Cancer Detec and Preven* 6(6): 515-525.
- Zhang Z, Wang Y, Yao R, Li J, Yan Y, La Regina M, Lemon WL, Grubbs CJ, Lubet RA, You M, 2004. Cancer chemopreventive activity of a mixture of Chinese herbs (antitumor B) in mouse lung tumor models. *Oncogene* 23(21): 3841-3850.
- Zhao L, Zhao A-G, Zhao G, Xu Y, Zhu X-H, Cao N-D, Zheng J, Yang J-K and Xu J-H, 2014. Survival benefit of traditional Chinese herbal

- medicine (A Herbal Formula for Invigorating Spleen) in gastric cancer patients with peritoneal metastasis. Evid-Based Complement Alternat Med 2014: 625493.
- Zhong WS, Ren T, and Zhao L-J, 2016. Determination of Pb (Lead), Cd (Cadmium), Cr (Chromium), Cu (Copper), and Ni (Nickel) in Chinese tea with high-resolution continuum source graphite furnace atomic absorption spectrometry. J Food Drug Anal 24(1): 46-55.
- Zhou Q, Chang B, Chen XY, Zhou SP, Zhen Z, Zhang LL, Sun X, Zhou Y, Xie WQ, Liu HF, Xu Y, Kong Y, Zhou LB, Lian FM and Tong XL, 2014. Chinese herbal medicine for obesity: A randomized, double-blinded, multicenter, prospective trial. Am J Chin Med 42(06): 1345-1356.
- Zimmerman BF, Walch SG, Tinzoh LN, Stühlinger W and Lachenmeier DW, 2011. Rapid UHPLC determination of polyphenols in aqueous infusions of *Salvia officinalis* L. (sage tea). J Chromatogr B Analyt Technol Biomed Life Sci 879(24): 2459-2464
- .Zotou A, 2012, An overview of recent advances in HPLC instrumentation. Central Eur J Chem10(3): 554-569.