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The Untold story of Herbal Medicine behind the current research: An overview of the efficacy, safety and interaction with the alternative medicine

Sanjay Kumar Verma[1*], Smita Kadu[1]
1. Department of Kriya Sharir, Dr. D. Y. Patil College of Ayurved & Research Centre
Dr. D. Y. Patil Vidyapeeth, (Deemed to be University), Pimpri, Pune – Maharashtra, India-411018
Corresponding Author's Email: sanjayvermamzp@gmail.com

ABSTRACT

Ayurveda is an ancient system of medicine that originated in India even been practised since 1500 BC; the main aim of this system is to the preservation of normal health and cure the disease by focusing on patient safety and benefits. In fact, it is commonly believed that the safety of every individual is a very basic and known fundamental concept in herbal medical practice. In the modern era, the present issue is raised concerning the Adverse Drug Reactions (ADRs) while concomitant use of alternative medicine with herbal medicine. As we know the open truth, after the pandemic, the use of herbal medicines continues to expand rapidly across the world not only as a remedy of bottom line cure of disease even improvement of self-strength as immunity while considering alternative medicine system as symptomatic relief remedy. Since long ago herbal medicines are found to be safe while the number of Adverse Drug Effects (ADE) is associated with alternative medicine. The main reason behind reported interaction was either self-medication, presence of inorganic impurities or prescribing alternative medicine by a Register Allopathic Medical Practitioner or Practitioners related to another medicinal system, without consultation with a registered Ayurvedic Medical Practitioner. In response to this attempt, it is difficult to describe the comparative pros and cons of the available medicinal systems but this review bears the impression of footsteps of the safety of herbal medicines while an attempt has been made to cover the untold story behind the reported researches related to said ADRs.

***Keywords**: Ayurveda, Herbal drug interaction, Safety of herbs, Self-medication, Toxicity of herbs, Adverse drug reaction, Inorganic impurity*

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INTRODUCTION

The use of herbal medicine to cure human diseases and ailments at the causative root has been coming from ancient cultures, generally, Ayurvedic medicine practitioners used extracts from plants to soothe and relieve aches and pains. Herbal medicinal plants and herbal plant products are known as 'Ayurveda'. Ayurveda is one of the ancient, most renowned and frequently used traditional systems of medicine based on the herbal product technology that has survived and flourished for ages to date. It is believed that Ayurveda has an age-old history since the 2nd Century BC while its foundations were laid by the Hindu Philosophical teachings named 'Vaisheshika" and the school was named 'Nyaya'[1-3]. Ayurveda has a rich history because of the magical effect exerted by herbal medicine. Let us start to express our beliefs in the herbal medicinal system with the magical activity of one magical plant known as *Sanjeevani* in Hindi. According to Ramayana,*Sanjeevani*has remained a part of the cultural heritage for several millennia in India, Thailand, Indonesia, Cambodia, Nepal, Srilanka and other sub-continent certain neighboring countries. Since long ago it believed that the term the *Sanjeevani*in itself consists of 'Jeeva' means 'Life' or expressed to denote something that offers life. The epic story of Hindu mythology "Valmiki Ramayana'is mentioned in Yudhakandprakaran that when Lakshman got injured and fell unconscious even seems to become dead or near to death by a fatal attack with poisonous "Mantraputa" arrows on the battlefield,The Royal physician 'Susena' directed Hanuman to step Dronagiri hills and bring four plants named as '*Mritasanjeevani*', for reviving life of Laxman, '*Vishalyakarani*', for removing arrows from his body, '*Sandhanakarani*', for restoring damaged skin and *Suvarnyakarani* for restoring skin colour. It was also mentioned that just after smelling the combination of revitalizing medicinal herbs, Lakshmana gained consciousness. It is a well-known fact that most of the plant species that exist in nature possess various medicinal properties. Hence it seems that '*Sanjeevani Booti*', is one of the ancient majestic herbs that have

the capability of resurrecting the life of every individual without any ADE [4,26, 73]. In A.D. 1655, John Goodyew translated the first reference from the term '*Dioscorides Medical treatise De MateriaMedica*' into English terminology as use of *Aloe vera* while in the early 1800s it was successfully used as laxative whereas in the mid-1930s it was used for chronic and severe radiation dermatitis. The history of various countries including Greece, Egypt, India, Mexico, Japan and China has shown an impression of the footprint for use of the ancient wonder herb '*Aloe vera*' for the different ailments or diseases even proved its efficacy and safety profile. Egyptian queens Nefertiti and Cleopatra regularly involved the use of this wonder plant in their beauty regimes whereas Alexander the Great, and Christopher Columbus used it to treat their soldier's wounds. The modern therapeutic approach for beauty enhancers also lists *Aloe vera* as the most favourable and safe plant in cosmetic industries. In the ancient system of herbal medicine, various herbs have been known for centuries for their unique medicinal properties, but now it has been rediscovered and recognized and are benefiting people's health with great safety. The active ingredients hidden in the plant extracts have the power to soothe human life and health in myriad ways. Herbal formulations areundoubted, nature's gift to humanity and it remains for us to introduce them to ourselves and thank nature for this never-ending gift [28]. The ancient science of herbal medicinal system especially cosmetology is believed to have originated in Egypt and India only, but the earliest records of substances used as cosmetic and their application dates back to Circa 2500 and 1550 B.C, to the Indus valley civilization [35]. There is several evidence of highly advanced ideas related to self-beautification reported in the history of various countries that have proven the safely use of a large array of various herbal cosmetics by both men and women. In ancient India, as per belief and mentioned in history that the use of herbal cosmetics was subtly interwoven with the seasons also known as *Rutus* in Sanskrit and the normal rituals of life as *Dinacharya in* Sanskrit. In this context, it is necessary to pay attention to the earliest even major example of self-beautification is from the great epic Mahabharata, where the Pandavas were in exile incognito. Draupadiwas the queen of Virata Rajvansh currently known as the Northern district of India, she called herself Sairandhri because she always believed in beautification even though it was reported that her an attendant in the women's sections of the palace of ViratRajya, always carried a box known as Prasadhana Petika containing a variety of herbal substances of beautification, toiletries and accessories to decorate herself, especially her hair. Although there was no evidence mentioned about ADE related to herbal substances in that era while using them frequently because of their wide safety profile. Significantly, the use of herbal cosmetics in the modern era with the time was directed people not only toward developing an outwardly pleasant and attractive personality but also promoting them towards achieving pure souls, the merits are mentioned in the Sanskrit language in the various Indian '*Veda' or 'Granths*': Always be good and do good for all (Sanskrit: *Punya*), Longevity with good health(Sanskrit: ***Aayush*** and *Aarogyam*) and Happiness (Sanskrit: *Anandam*) [55].

This past decade has been considered an open truth even found to be witnessed a tremendous surge in acceptance and public interest in natural or herbal based therapies both in developing as well as developed countries. In the developed countries, the major reason among many other reasons for selecting and adopting herbal therapy is the belief that it will promote healthier living even found to be true. Herbal medicines are, therefore, often believed and viewed as a balanced as well as a moderate approach toward healing or bottom line cure of the disease or ailments and every individual using them as home remedies and consider as over-the-counter drugs even spend a huge amount of money (more than billions of dollars) on herbal-based products. Thus the sale of herbal-based medicines is booming day by day and represents a substantial proportion of the global drug [6, 7, 32, 53]. The use of herbal-based medicines and their phytonutrients to expand rapidly across the world with many people now resorting to these products for the treatment of various health challenges, ailments or diseases in different national health-care settings. While some other places in the world like the UK have a historical tradition of using herbal-based [49], the use of herbal-based products is also widespread and well established in some other modern European countries [14]. The embracing fact behind the use of herbal remedies in many developing and developed countries including India is 'availability', these herbal remedies are available not only online but now also in food stores and supermarkets instead of drug stores even can be purchased without a prescription. It is estimated that around 80% of the world's population representing four billion people living in the developing world now rely on herbal or plant-based medicinal products as a primary source of healthcare [6, 10, 55, 54, 45]. This leads to self-medication either alone or with the concomitant use of modern or other medicinal systems; hence, the chances of ADR might be increased. In the modern era, as the global use of herbal-based continues to grow with age and many more new products are aimed to introduce into the global market, public health issues, and their safety is also considered. Although it was reported that some herbal medicines have promising potential and are widely used in the current era, many of them remain untested and their use is also not monitored by researchers. Attention also be paid to the major factor is the lack of suitable

quality controls (Extraction and Isolation), use of additives that are rich in lead, arsenic and other impurities, inadequate labelling, the absence of appropriate patient information, and guideline to use [59]. Although herbal medicines are believed to be safe, some practitioners of other medicinal systems who don't have extended knowledge about it, continuously prescribe herbal medicine with modern medicine as adjunct therapy even self-medication by some of the population, making herbal medicines dangerous to themselves or other human beings. Also must be noted that some Registered Ayurvedic Medical Practitioner prescribe allopathic medicines with herbal medicine without evaluating related ADR, also be responsible for the same. The negligence of Registered Ayurvedic Practitioners is the main reason behind the present controversial debate about the harmful effect of herbal medicines. In the current era number of research and case reports were published related to the harmful effects of herbal medicines but seem to fail to focus on the basic reasons behind it. Now it has become essential, therefore, to furnish the general public including all the healthcare professionals with adequate information to facilitate a better understanding of the efficacy, risks associated with the use of a herbal product as self-medication even concomitant use with the other products of the different medicinal system and to ensure that all medicines are safe and of suitable quality provided by the manufacturer. Based on the literature survey, we are trying to establish the basic reason as well as conditions behind the reported toxic and harmful effects associated with the herbal medicinal system.

Reported herbal drug interaction

With the wide and enormous knowledge of these available ancient nature-based herbal medicinal systems, the relationship of the human body's constitution and function to nature even the elements of the universe that also act in coordination with each other and affect the lives of living beings, although this system is continuing to flourish in ages even still to come. Since many avenues are still waiting to be explored by the practitioners, experts and researchers in the field of herbal medicine who carry the responsibility of keeping these herbal based ancient traditional systems of medicine alive and making continuous efforts for its growth in the future. It was reported that the distribution pattern of drugs like 9-Aminocamptothecin, daunorubicin, epirubicin, etoposide, lurtotecan, mitoxantrone, SN-38, topotecan is also affected through BCRP (ABCG-2, MXR) protein by flavonoid-containing herbs such as *Glycine max* (soybean), *Gymnemasylvestre*, and *Cimicifugaracemosa* (black cohosh) [66, 42]. Some of the researchers claimed that *Vacciniummacrocarpon* contains anthocyanins and flavonoids that have proven antioxidant activity but showed ADR when used with warfarin [44]. The effect of warfarin potentiate by garlic known as *Allium sativum* [11], Dong quai (*Angel-icasinensis*) [51] or danshen (*Salvia miltiorrhiza*) [15], with resultant in high bleeding. Another report published related to spinal subdural hematoma and the frontal intra-parenchymal hematoma was in a patient, who was in remission for two years with rituximab, hydroxychloroquine and warfarin, but she had been using some herbal products (shepherd's purse and horsetail) and phenyramidol from past few days. It was observed that spinal and cerebral hematomas were caused by the interaction between phenyramidol and warfarin [19]. The herbal product containing *Rosmarinus officinalis* may influence on transport proteins namely P-glycoprotein (ABCB-1, MDR-1) and hamper the distribution pattern of some drugs like actinomycin D, daunorubicin, docetaxel, doxorubicin, etoposide, irinotecan, mitoxantrone, paclitaxel, teniposide, topotecan, vinblastine, vincristine, tamoxifen, mitomycin-C, tipifarnib, epirubicin, bisantrene [47, 52] and *Curcuma longa* found to influence or change the distribution of etoposide, teniposide, vincristine, vinblastine, doxorubicin, daunorubicin, epirubicin, idarubicin, topotecan, irinotecan, mitoxantrone, chlorambucil, methotrexate, melphalan through MRP-1 (ABCC-1) protein [61]; while interacting with MRP-2 (ABCC-2) SN-38G (metabolite of irinotecan) change in the distribution ofmethotrexate, sulfinpyrazone, vinblastine [25]. The most widely used herbal medicine as an antidepressant is St John's wort [36]. It was found as a potent inducer of CYP3A4 and depending on the route of administration, duration and dose, it was reported that it may induce or inhibit other CYP isozymes and P-gp [60, 40, 67, 39] the interaction with CYP3A4 significantly reduces the plasma levels of CYP3A4 substrates including cyclosporine, simvastatin, indinavir, warfarin, amitriptyline, tacrolimus, oxycodone, and nevirapine [48, 69]. Also, the organ rejection was reported due to the alteration in the blood serum concentration of cyclosporine [22, 46] even some evidence of unplanned pregnancies was documented because of breakthrough bleeding due to interaction between St John's wort and oral contraceptives [29]. *Panax ginseng* (Ginseng) contains triterpene, saponins, ginsenosides widely used for loss of energy and memory improvement, stress and male sexual activity but interact with immunosuppressants and hypoglycemic agents and might be interfering in immunomodulatory and hypoglycemic activity [71], also reported that it induced mania in patients on antidepressants drugs [21]. Another major ADR reported with the use of *Ternstroemiapringlei* which contains essential oils and is used as sedatives and exert synergizing sedative and hypnotic action when used with sedatives and hypnotic's drugs even may be fatal in high dose [5]. The synergistic action also reported with *Digitalis lanata* contains acetyldigoxin, digitalin, digoxin, digitoxin, gitalin and anatosides known as positive

inotrope that increases cardiotonic activity cardiovascular drugs [72], while plant extract of *Aspilia africana* contains some alkaloids, tannins exert antagonistic action when prescribed with artemisinin or chloroquine [70]. The anticholinergic herbal medicine *Anisodustan guticus*is widely used in China but might interfere with other cholinomimetics drugs [23]. *Zingiber officinale*is commonly known as Ginger used for Nausea, dyspepsia, antiemetic, antiplatelet activity because contains wonder constituents zingerone andgingerols but reports to show ADR with diclofenac, anticoagulants and antiulcer drugs [74, 36]; while the ADRs was reported in a case report of a 76-year-old white European woman who was on long-term phenprocoumon therapy with an international normalized ratio and epistaxis within the therapeutic range, but once she began using products containing ginger, she developed an elevated international normalized ratio up to 10 and epistaxis after several weeks. The international normalized ratio returned to the normal range when ginger products were cut off as well as treated with vitamin K-1 [34]. The another commonly used herbal medicinal plant *Glycyrrhiza glabra* contains glycyrrhizinic acid indicated for gastric ulcer, catarrhs and inflammation but interact with antihypertensives and diuretic drugs to cause hepatotoxicity [4], Fatel et al mentioned in a case report of an 84-year-old man presented to the emergency department with a hypertensive emergency because of liquorice tea. [24], the same effect was observed ina 41 year old patient [13], while it was reported that it was also responsible to alter the metabolism of albendazole in patients with hepatic alveolar echinococcosis [12]. The use of herbal medicines is common among HIV-positive patients, even in those who are on antiretroviral treatment. Horsetail, known as "*Equisetum arvense*" is mainly used for its diuretic properties. It was observed in 2 cases of patients with an HIV-positive report, concomitant use of Horsetail with lamivudine or zidovudine or efavirenz or and emtricitabine or tenofovir, respectively, a possible drug-herb interaction may have led to a virological breakthrough and might be fatal [17].

DISCUSSION

The plants or plant-based products provide a desirable therapeutic effect with reduced risk or possibilities of risk of iatrogenic complications, such as side effects or adverse effects often associated with conventional medication. It was reported that the combined treatment of herbal medicines or herbal based products and synthetic drugs or alternative medicines may reduce some side effects or adverse effects of highly potent drugs [30, 3].

However, a major limitation on the use of herbal medicine or herbal-based medicine in the phytopharmaceutical area is the lack of consistency as well as purity in the levels of compounds present in the plant extract because of natural variability (presence of the various active constituents) due to inappropriate isolation of single active compound of desirable therapeutics use, leading to inconsistent results upon scientific validation [18]. Also, another major limitation is the failure in the reproducibility of the reported activity by more than 40%, when using herbal-based products containing plant extracts, as the activity detected often does not occur when re-extracted samples are tested again or validated for the same activity [33, 58, 1, 2]. This problem may beassociated with the cultivation and collection process, differences in the biochemical profiles of plants always encountered when harvested at different times and locations, also the variations in the same genus plant and variations in the methods used for the extraction or isolation even determination of biological activity (Ahmad et al., 2006,Raskin et al., 2002b). The principles of phytotherapy or herbal based medicinal system, a plant may contain several pharmacologically active chemical constituents or compounds that must be seen as a single unit [53]. It is another limitation and challenge for pharmaceutical formulation to either standardize the entire extract or isolate single constituents with the purity of desired activity and can be clinically tested for a particular clinical condition [43]. Nowadays, Indian medicinal plant extracts or herbal based products have been considered as a potential source of heavy metal toxicity to both man and animals (Dwivedi and Dey, 2002). The most common heavy metals which were detected when analyzed analytically even are arsenic (As), lead (Pb), cadmium (Cd) and mercury (Hg) although nickel (Ni) and chromium (Cr) may cause ADRs, adverse effects even responsible toxicity or fatal action. In India, the Ayurvedic Pharmacopoeia of India recommends that medicinal plants, which are used as raw materialsfor herbal formulations, must be analyzed for the presence of the above said heavy metals especially should bewithin the prescribed limits for them. However, it was found that most Indian Ayurvedic and herbal companies procure the herbal raw material from commercial suppliers and use them in formulations without checking or analyzing them for the presence of heavy metals as well as their quantity. In the reported study it was found that the marketed formulation of herbal plant extract of *Embelicaribes*detectedAs-0.62, Pb-1.01, Cd- below 0.05, Hg- below 0.05, Cr-1.41 and Ni-0.41ppm respectively, the formulation is considered as a rich source of inorganic impurities which found above then the prescribed limit is As, Pb, Cr and Ni while another formulation of *Zingerofficinalis* containedAs-0.53, Pb-1.32, Cd- 0.06, Hg- below 0.05, Cr-1.89 and Ni-0.50 ppm, inorganic impurities such as As, Pb, Cd and Ni found in higher limit than prescribed. Further, it was

found that plant-based product of *Asparagus racemosus* analyzed and confirmed the presence of As-0.07, Pb-0.94, Cd- below 0.05, Hg- below 0.05, Cr-1.18 and Ni-0.61 ppm respectively, except Cd and Hg, it was reported that As, Pb Cr and Ni were in upper limit than prescribed. *Glycyrrhizaglabra* based herbal product showed the presence of As-0.13, Pb-0.98, Cd- 0.08, Hg- 0.06, Cr-2.04 and Ni-0.77 ppm, all the major toxic impurities were in the upper limit while *Emblicaofficinalis* detected As- below 0.05, Pb-0.72, Cd- below 0.05, Hg- below 0.05, Cr-0.79 and Ni-1.08 ppm, at least major harmful As was found within the prescribed limit with Cd and Hg but rest of major impurities were detected in higher limit. The published report also analysed various samples of herbal based products and sowed that plant-based products contained all the major inorganic impurities in upper limit in different formulation such as *Terminaliaarjuna*- As-0.35, Pb-1.06, Cd- below 0.05, Hg- below 0.05, Cr-1.96 and Ni-0.58 ppm, *Chlorophytum borivilianum*- As-0.09, Pb-0.89, Cd- 0.07, Hg- below 0.05, Cr-2.18 and Ni-0.65 ppm, *Curcumaangustifolia* -s-0.06, Pb-1.28, Cd- below 0.05, Hg- below 0.05, Cr-1.20 and Ni-0.47 ppm, *Picrorhiza. kurroa*- As-0.41, Pb- 0.96, Cd- 0.05, Hg- below 0.05, Cr-1.56 and Ni-1.12 ppm respectively, *Piper longum*- As- below 0.05, Pb- 0.68, Cd- below 0.05, Hg- below 0.05, Cr-3.08 and Ni-0.34 ppm respectively [8].

Clinical implications associated with inorganic arsenic are much known worldwide as a health problem, although Arsenical species vary in their degree of toxicity that maybe associated with hematologic and cardiovascular disease, the actual cause and mechanismare currently unknown (Lee et al., 2002). Arsenic compounds mainly existin the inorganic and organic forms and state of pentavalent and trivalent oxidation, it was reported that inorganic compounds are more toxic than organic There would be possibilities of some inter-conversion between the less toxic species of arsenic because of manufacturing conditions [41]. Some of the clinical features associated with inorganic arsenic impurities mainly associated with the gastrointestinal tract are nausea, vomiting, colicky abdominal pain, and profuse watery diarrhoea. Other clinical features are renal failure, respiratory failure with pulmonary oedema, acute psychosis, skin rash, haematological abnormalities, toxic cardiomyopathy, seizures and metabolic changes. In concern with metabolic change, it was investigated that arsenic exerts its toxicity by inactivating more than 200 biological enzymes, especially those involved in DNA synthesis and repair as well as cellular energy pathways [50]. The toxic effects associated with inorganic are well known since it has been used for thousands of years but there remains considerable debate about the health effects associated with it even in low-level exposure. There is no doubt that further qualitativeand quantitative research is needed because a narrow margin between safety and toxicity. The clinical features associated with lead exposures are peripheral neuropathy, neurocognitive deficits, hypertension, nephropathy, anaemia, and sperm abnormalities. In metabolic concern lead also inhibits some enzymes and stimulates the synthesis of binding proteins in kidney, brain, and bone, causing alteration in cellular calcium metabolism and slowing down nerve conduction [54, 27]. The greater acute health effects of mercury salt have been reported than elemental mercury because Mercury salts are found to be more corrosive than elemental mercury, which increases gastrointestinal permeability and absorption for other macromolecules. An acute high dose exposure of mercuric salts primarily causes corrosive damage to the gastrointestinal tract and leads to darkened discolouration of the oral mucous membrane and severe gastrointestinal symptoms with burning chest pain. Mercury salts are generally irritants on the skin that cause discolouration of the nails, corrosion of the mucous membranes, dermatitis, and may also cause corrosive burns, The proximal convoluted tubules in the kidney is reported as the major target organ of inorganic mercury and may cause polyuria and proteinuria (especially low molecular proteinuria), with hematuria and anuria [54, 9, 65].The history of nutritional and biochemical studies of the necessary elements of the human body is unfortunately full of twists and turns even some of the most leading to dead ends likely chromium exist as the trivalent ion, which has been proposed to be an essential element for various biological relations, a body mass and muscle development agent, an agent to increase insulin sensitivity and affect lipid metabolism, although a molecular mechanism for such actions has not been elucidated while the most popular chromium-containing nutritional supplement is found to be toxic when given orally to mammals. In the current era, chromiumis found less toxic and safe than the prescribed limit even the body can tolerate it at a higher limit also. [62, 68]. Discussion in this current debate is limited to toxicity-related health issues and major safety concerns arising from the concomitant use of herbal medicines with alternative medicine. As we know the utilization of herbal based products increasing day by day as self-medication either by individuals or patients without any concern forth presence of inorganic impurities such as arsenic, nickel, cadmium, chromium and lead that cause serious clinical complications even might be fatal. Since the number of researches reported related to herbal-drug interaction and always trying to claim herbal-based medicines interact with alternative drugs and cause ADRs. But surprisingly it was found that researchers ignored the presence of impurities in either semisynthetic, synthetic, or herbal products that may be responsible for said ADRs because in every

reported research it was found that there is no explanation of labelling even description of present impurities in the product used. In the various reported research related to herbal drug interaction, there is no consideration of whether the herbal product contains a single isolated form of a particular chemical constituent or used plant extract, although plant extract is basically a mixture of various chemical constituents, therefore researchers still need to expand their research first before claim above said interaction. Also, there may be chances of other reasons such as patients being uncomfortable or feel hesitation about discussing their medical problems because of lack of confidentiality regarding handling their health information, possible misdiagnosis even wrong treatment or dietary factors by patients with non-specific symptoms or general malaise, also note that lack of time to take for proper diagnosis by a physician. Furthermore, providers of herbal medicines are a big issue for this reported interaction because a variety of healthcare professionals serve as qualified providers of herbal medicines, especially physicians but unfortunately in some countries, community pharmacists are always ignored in their job, although community pharmacists are normally qualified providers of herbal medicines, who are the well trained, have knowledge about efficacy, safety and possible drug interaction. Health-care professionals related to other medicinal systems who are not providers of herbal medicines are also likely to be poorly informed or trained about herbal-based products and how they are being prescribed or used even they also try to ignore Registered Ayurvedic Practitioner [64]. There is no doubt that cases associated with poisoning due to the presence of inorganic impurities in the herbal medicines which are available in the market, is necessitating the need to ensure to maintain quality of herbal based products alongside active pharmacovigilance should be established on these products to promote their safe as well as effective therapeutic use and protect public health [20]. None of these proposals related to the harmful effect of inorganic impurities despite significant attention in the popular media while reporting herbal drug interaction, however, herbal-based products were found to be a rich source of it and have proven to be correct.

CONCLUSION

The safety of herbal based products is the likelihood of not causing harm to the patients under the proposed conditions of use (When the presence of inorganic impurities were present within the prescribed limit), while efficacy is the capacity of individual medicinal substances to induce a clinical benefit. It is most important to focus and determine whether said ADRs are caused by the way an herbal based medicinal product has been used or prepared. Particular attention to these factors should be given when and under which conditions herbal-based products are prescribed or consumed as self-medication without concern of impurities present, misdiagnosis and prepared or prescribed by poorly trained providers or unqualified physicians and practitioners, all above said factors are responsible for unsafe use even may lead to overdose and ADRs. Also, a change in the procurement sources, misidentification of the medicinal plant and plant material used, manufacturing process, use of additives that contain stem inorganic impurities, and quality control including uncontrolled cultivation, collection, extraction and isolation with inappropriate quality control methods of herbal materials, or a change in the mode of preparation may lead to possible ADRs. This should be taken into account whenever assessing individual cases and recommended to established standards of practices. In the various reported research related to herbal drug interaction, there is no consideration of whether the herbal product contains a single isolated form of a particular chemical constituent or used plant extract, although plant extract is basically a mixture of various chemical constituents, therefore researchers still need to expand their research first before claim above said interaction. Another main reason behind reported interaction was either self-medication, presence of inorganic impurities or prescribing alternative medicine by a Register Allopathic Medical Practitioner or Practitioners related to another medicinal system, without consultation with a registered Ayurvedic Medical Practitioner. In response to this attempt, it is difficult to describe the comparative pros and cons of the available medicinal systems but this review bears the impression of footsteps of the safety of herbal medicines while an attempt has been made to cover the untold story behind the reported researches related to said ADRs.

The famous Latin expression “primum non nocere” (“first, not do harm”) must be come first in planned therapeutic interventions, also, the classical version of the Hippocratic Oath must be opted by all the physicians which stated that “physicians take upon entering medical practice contains a promise that expresses a similar idea (doctors are required to “keep [patients] from harm”)”.

Ayurveda is one of the most renowned and ancient plant-based traditional systems of medicine that has flourished and survived from ages till date, although there are many avenues still to be explored by the practitioners, experts and researchers, in the field of herbal-based medicine who carry the responsibility of keeping this ancient traditional system alive and contributing to the growth in the future.

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