Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(5), 430-438 | ISSN:2251-6727

Efficacy Of Herbal Drugs and Cost-Effectiveness

Ujjwal Nautiyal[1]*, Rahul Pandey[2], Abhishek Chandola[3]

[1]*Swami Rama Himalayan University, Himalayan School of Pharmaceutical Sciences, Jollygrant, Dehradun.
Email ID: -ujjwalnautiyal@srhu.edu.in
[2]Swami Rama Himalayan University, Himalayan School of Pharmaceutical Sciences, Jollygrant, Dehradun.
[3]Swami Rama Himalayan University, Himalayan School of Pharmaceutical Sciences, Jollygrant, Dehradun.

***Corresponding Author:** Ujjwal Nautiyal
*Swami Rama Himalayan University, Himalayan School of Pharmaceutical Sciences, Jollygrant, Dehradun.
Email ID: -ujjwalnautiyal@srhu.edu.in

KEYWORDS
Herbal Drugs
Cost Effectiveness
Efficacy of Herbals

ABSTRACT:

Since times immemorial, mankind has relied on herbs and plants on natural origin to alleviate its sufferings. Irrespective of the geographical separation among different civilizations, the dependence on plants for treating diseases and ailments was common to all settlements. The ethnopharmacological basis of various existing drugs is well established. With advancements in science and technology, the herbal medicines have also seen a transition from galenicals, pills, extracts to high end herbal capsules and other refined formulations. Inspite of meteoric rise in the sale and composition of herbal medicines around the globe, there have always been questions on the efficacy and cost effectiveness of these remedies. This chapter will focus on the scientific and well documented cases of efficacy of such drugs and also provide a commentary on their cost effectiveness. Attempts will also be made to compare the costs with other lines of treatment and their associated side effects. Further, the safety and toxicity of herbal drugs and their interaction with allopathic drugs will also be discussed.

Objectives:

- Understanding the historical development of herbal drugs
- Understanding the benefits of herbal drugs
- Assessing the cost effectiveness of herbal drugs
- Understanding the various herb-drug interactions
- Exploring the reasons for toxic effects of natural medicines

1. Introduction

Herbs and their isolated phytoconstituents have beneficial effects for human disorders since ancient times. Herbal therapy was only remedy available from the early days of civilization and people these days are enthusiastic about the use of herbal medicine [1]. Plants are known to occur on the earth around 500 million years ago and approximately 400000 species have been identified and sub-classified to date [2]. The traditional treatments through medicinal plants are the main source for treating severe disorders [3].

The development of some of the herbal remedies can be attributed to serendipity. Nevertheless, recent modern medicine scenario is not incidental but based on primary herbal research screening processes. Recent trends involve utilization of Ayurvedic or natural remedies approved by Food and Drug Administration (FDA) for screening of new isolated phytocomponents from natural sources [4]. In different natural medicine systems, a prescription often comprises several ingredients compositing into a given ratio in an each formula, wherein each component in isolation sometimes lacks therapeutic activities seen in the holistic formulation, a phenomenon known as the combinatorial effect [5].

The trust of patients towards traditional medicine system stems from various attributes. Such remedies are often easily available, are easy to use, cost effective and possess low side effects and help to improve overall health [6]. Although, in rural settings, non-availability of professional care and infrastructure may also promote the use of home remedies for acute and self limiting pathophysiological situations [7]. However, home medication and combination of herbal drugs without medical expert may be harmful to patient health. In this context, government regulatory bodies are required to

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(5), 430-438 | ISSN:2251-6727

check all safety parameters with respect to public health for home medicine use by itself [8]. A huge numbers of herbs have proved their effectiveness in acute diseases along with their utilization in severe chronic disorders. Hence for the development of successful herbal therapies, it is imperative that the mechanism(s) of herbal drug effect are clarified for the knowledge of all stakeholders [9].

This chapter will be focusing on benefits of herbal medicines with respect to public health. This work will also focus on the scientific and well documented cases of efficacy of such drugs and provide a commentary on their cost effectiveness. Attempts will also be made to compare the costs with other lines of treatment and their associated side effects. Further, the safety and toxicity of herbal drugs and their interaction with allopathic drugs will also be discussed.

2. Benefits of herbal drugs

It is a matter of common debate that why herbal medicines are better than modern medicine. Another school of thought often propagates the superiority of modern medicine over traditional drugs of natural origin. The herbal medicine gains an edge because of its cost effectiveness and easy to use as home medicine. However a thorough point wise discussion is presented below:

2.1 Cost effectiveness

Popularity of herbal drugs over modern medicines due to their low toxicity and less cost is well known. Traditional Chinese medicines promoting the uses of natural products for public disorders have been proved cost effective. For example, Jingshu granules have cost effective approaches to treatment of cervical radiculopathy in China [10]. According to World health organization (WHO) approximately eighty percent population looks forward to traditional medicines for treatment of diseases. However, only fifty countries have made national policies governing the use of traditional medicines which include China, Japan and Germany. In India, the use of Ayurvedic or traditional substances has been regulated through 'Drugs and Cosmetic Act of 1940'. In 1959, the government of India amended the Drugs and Cosmetic Act to include the natural products derived from plant sources [11]. Low cost of herbal drugs has always been alluring the users towards health benefit in respect to allopathic medicines. The regulatory bodies around the globe have been hard pressed to carry out standardization of natural products through proper clinical trials. Although, in different developing countries it is difficult to maintain the quality standards for crude extracts but the need for standardization cannot be undermined [12]. **Table 1** presents a comparative account of traditional medicine systems with modern systems of medicine along with their cost comparison.

Table 1: A comparative account of cost effectiveness of herbal medicines vis-à-vis different traditional medicine systems

S.No	Type of Disease	Comparison between herbal drugs versus modern drugs treatment system					References
		Traditional Medicine System			Modern Medicine System		
		System of medicine	*Name of Herb*	*Approximate Cost of Therapy (In Dollar $) / Duration of Therapy*	*Name of Modern medicine*	*Approximate Cost of Therapy (In Dollar $) /Duration of Therapy*	
1.	Cervical Radiculopathy	Chinese Traditional Medicine	Jingshu granules	179.90/4-weeks	Qishe Pill	1143/4-weeks	10, 64
2.	Diabetes Mellitus	African Traditional Medicine	*Buchholzia coriacea*	745/Annually	Jardiance	16,752/Annually	65, 66
3	Obesity	Indian Ayurvedic Medicine	Guggul	23/4-weeks	Orlistat	80/4-weeks	67
4	Cancer	Traditional Japanese Medicine (Kampo)	*Agaricus blazei* mushroom	500/4-weeks	Lenalidomide	5,282/4-weeks	68
5	Insomnia	Chinese Traditional Medicine	*Glycyrrhiza uralensis*	30-60/4-weeks	Tian Meng oral liquid	17,281/4-weeks	27, 69, 70
6	Allergic Disorders	Traditional Japanese Medicine (Kampo)	*Sophora flavescens* (Alkaloid-Oxymatrine)	21.95/4-weeks	Ninjin'yoeito	3817/4-weeks	71
7	Hematological Disorders	Indian Ayurvedic Medicine	Lauhasava	6/4-weeks	Cyanocobalamin (Vitamin-B12)	14/4-weeks	72

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(5), 430-438 | ISSN:2251-6727

In India, a large number of people are suffering from chronic disorders like diabetes, obesity and cancer. Often these severe chronic diseases come with economic burden to people. As per an estimate, treatment of diabetes mellitus accounts for 14.2 % of total health care costs [13]. Similar to diabetes, obesity has also been increasing the economic burden of health care cost of patients in both developed and developing countries [14]. The increasing cost of prescription drugs has prompted people to look for alternatives in herbal drugs which cost less as compared to allopathic medicines. Continued use of herbal remedies helps patients to manage conditions and undertake preventive measures that reduce chances and severity of illness and promote selfhealing. The knowledge thus gained can be used to lead a better and healthy lifestyle keeping chronic conditions at bay and thereby saving on health bill [15].

2.2 Accessibility

The use of herbal remedies is not limited to therapeutic effect but herbs are also widely utilized for cosmetics and local skin related infections [16]. Over the counter products available as herbal extracts, essential oils and herbal tea are found effective in a number of ailments. Thus healthcare cost on obtaining consultation and prescription can be saved [17]. Not only herbs but also species, which are routinely available in the kitchen are also effective in different diseases, like turmeric, clove, cinnamon and chillies may act as potent medication to various allergic and infectious diseases (**Figure 1**) [18].

2.3 Wider therapeutic index

The conventional drugs having less adverse effects as compare to synthetic medicines for treatment of different disorders. However, 'Over the counter' (OTC) drugs such as indomethacin, warfarin, aspirin and Naproxen are associated with minor to major adverse effects like excessive bleeding and difficult breathing [19]. Natural drugs like opiates can be used as analgesic drug and isolated phytoconstituent from digitalis plant may be used for the treatment of heart related disorder like heart failure without major toxic action for organ system [20, 21]. Although, serious disorders like cancer may also be treated through natural substance like taxol with minimum side effects [22].

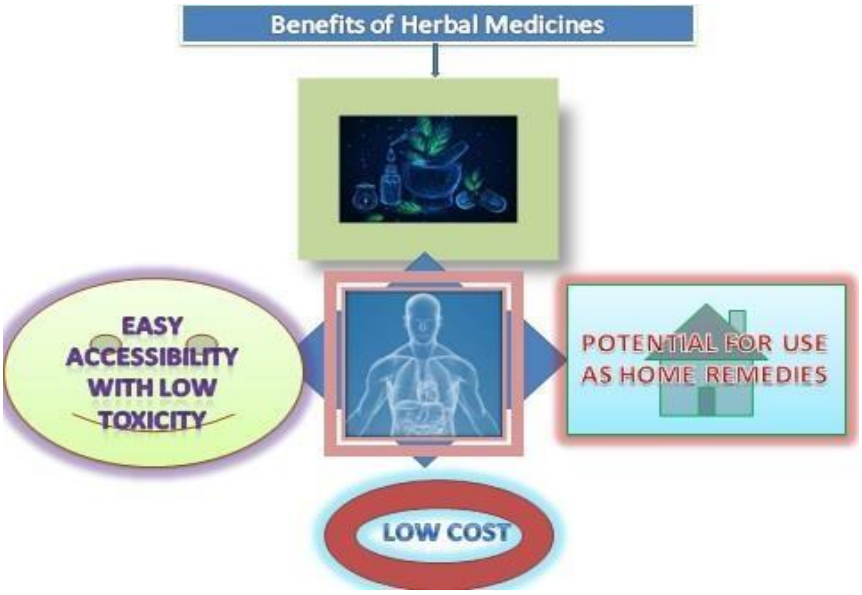

Fig. 1: Elaboration of herbal medicines used by human society

2.4 Self healing

It is often alleged that allopathic drugs mask the symptoms and do not permanently treat the underlying condition. On the contrary, herbal medicines or alternative drugs are alleged to act through placebo effects and patient may get on the path to better health sooner than expected [23]. However, not all herbal drugs producing placebo like effects as evident through the use of

FDA approved psychotropic natural agents against mental disorders like depression and anxiety [24].

2.5 Improve overall health

There has been a tremendous interest in natural medicine around the globe with concomitant huge increases in last few decades and present market of herbal medicine is approximately hundred billion US dollars [25]. Natural herbs have been used for severe and acute diseases like cardiovascular disease, prostate problems, depression, and inflammation and weakened immune system [26]. Herbal drugs have come with several remarkable health supports. The primary goal of folk medicines is to identify and eradicate illness rather than suppress the

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(5), 430-438 | ISSN:2251-6727

symptoms. This approach is more likely to result in improved health than the use of pharmaceuticals. In this context, the traditional Chinese medicine *Glycyrrhiza uralensis* was reported as a therapeutic drug for insomnia treatment [27]. Additionally, Ginko (Ginkobiloba) is good for circulatory disorders, but it also helps enhance memory [28]. Another conventional drug restrains vitamins, antibodies and other health-promoting agents; it serves to strengthen the overall body and not just combat illness [29].

3. Safety issues for herbal medicine use

Despite the popularity of herbal drugs increasing day by day, there have always been doubts about their safety and effectiveness. The general idea that herbal drugs are very safe and free from side effects is false [30]. According to scientific literature data, there are the two kinds of adverse issues *viz.* intrinsic and extrinsic. The former is concerned with predictable toxicity, over-dosage and interaction with conventional drugs, as reported for modern medicines and the latter is linked to several manufacturing problems such as misidentification of plants, lack of standardization, dereliction of good manufacturing practice, contamination, substitution and adulteration of plants, incorrect preparations and/or dosage, etc [31]. International Union of Pure and Applied Chemistry (IUPAC) Technical have published herbal protocols related to different aspects of scientific assessment of natural product formulation. In this document, various aspects of the science of herbal medicine in modern times have been compiled in one place and it is expected to significantly advance the scope of scientific assessment of herbal products prepared following certain standards [32].

However, toxicity issues of herbal drugs have been challenging task for scientific community. The contamination of herbal products due to various reasons for example misidentification, manufacturing malpractices, intentionally or accidental contamination [33].

The safety issue always has to be essential indicator for herbal drugs use by human community.

3.1 Complexity of safety of herbal medicines

The adverse drug reactions arising out of the use of herbal medicines are mainly classified in to two types *viz.* direct and indirect toxicity.

3.1.1 Direct toxicity

It can be occur due to overdose or even therapeutically normal dose of herbal medicines. Different patient groups have different levels of susceptibility for natural drugs use. For example, pregnant women and children experience profound herbal drug toxicity. Children and infants are more sensitive to herbal toxicity than adults [34]. Different scientific studies have explored the adverse effect originating by use of herbal drugs, such as podophyllin toxicity due to *Podophyllum emodi*, kidney fibrosis related to *Aristolochia fangchi* [35, 36].

3.1.2 Indirect toxicity

Some of natural agents may contain toxic ingredients those are responsible for toxic effect. The natural oil *Mentha pulegium* is known to contain an abortifacient content, which can induce hepatic and renal injuries [37]. Similarly, the natural herb *Morinda citrifolia* juice may be producing heart related disorders due to hyperkalemia effect into the renal system because it is containing high level of potassium ions in the natural juice of herb [38]. However, the environmental contamination of the herbs can be responsible for toxic action. The Chinese traditional medicines having high heavy metals in the herbs that are responsible for lead toxicity [39]. Furthermore, intentional adulteration can also be responsible for herbal toxicity. For example, *Echinacea* is the one of important herb used as anti-inflammatory and for relief in cold in US market. Wallace et al. reported that *Echinacea* is often adulterated by mixing of walnut, which can bring about allergic reaction by nut allergy [40].

3.2 Herb-drug interactions

The natural medicines are often supplied in the form of admixture of two or more active constituents. Multitude of active ingredients will increase the possibilities of interactions between herbal medicines and conventional drugs. However, herbal medicines interactions may also originate due to both pharmacokinetic and pharmacodynamic level of herb-drug interactions [41]. For example, herb-drug interactions can decrease absorption of the drug. A study has reported that the patients have suffering from angina related ischemic disease who taking aspirin along with *Ginkgo biloba* herbal extract, are likely to suffer from retinal bleeding because their interaction can lead to increased eye bleeding [42].

3.3 Reasons for toxic effects of natural medicines

3.3.1 Self treatment

Main cause of herbal toxicity is self-treatment due to easy availability of natural agents as homemade remedies. Herbal treatment without supervision has been always harmful. However, the correct drug administration and public awareness for safe use of natural drugs by Food and Drug Administration may play an important part for the prevention of herbal toxicity [43]. Herbal drugs used as supplementary dietary elements can produce hepatic and renal toxicity [44]. Obesity is the main health issue at Mexico, especially in women. One study report has related that

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(5), 430-438 | ISSN:2251-6727

approximately more than 40% of obesity to high prevalence of consumption of natural products [45].

3.3.2 Unqualified practitioners

Majority of natural drugs may be used as dietary supplements and the Dietary Supplement Health and Education Act of 1994 regulates it. Aforesaid law has to be exempt for prescription and regulation of OTC herbal drugs sales in the market [46]. Mostly herbal liver toxicity reported by self-medication or without supervision of qualified practitioners. This is challenging task for providing best health services in rural area because unqualified medical practitioners who do not possess any kind of recognized medical qualification are the only health providers in village areas [47].

3.3.3 Substandard Product

The vernacular names for herbal remedies can be outdated and misleading to identify correct drugs according to geographical region [48]. Substances that do not qualify quality and quantity parameters according to official herbal monographs are known as substandard products [49]. During formulation of herbal drugs at manufacturing unit accidental contamination of substandard heavy metal like lead, mercury, cadmium, and arsenic are responsible for intoxication for natural product quality [50]. There are four main reasons for adulterations in herbal products *viz.* undeclared synthetic products, synthetic pharmaceuticals, with undeclared heavy metals, placebo herbal medicine without active ingredients and herbal drugs with wrong active ingredient [51].

3.3.4 Improper intake

In the era of digital marketing and easy reach through social media platforms, there are a lot of misleading advertisements for herbal drugs. If the individuals consume these medicines without the advice of physician or registered practitioners, it is dangerous to patient health. Whereas there exist stringent quality control and good manufacturing requirements for modern drugs which are further passing through different trial phases. All information related to synthetic drugs treatment and its adverse reactions with suitable dose is enlisted into their leaflets [52]. Nevertheless, these procedures are not strictly followed in case of natural medicines. Although several herbal agents can be used as dietary supplements and may be sold without any specific directions. Sometimes expiry date is missing on the labels of herbal formulation and people continue to use such products over long period. All these factors are responsible for herbal toxic effects and it may be harmful for human health [53].

4. Precautions using herbal medicine

Individuals who are keen to take herbal supplements must consult a qualified health professional who can guide them about proper dose, associated potential side effects, and possible herb drug interactions. Some of scientific studies have reported that mild to serious side effects may occur when herbal drugs are consumed with conventional medicines. The fact that herbal drugs are always safe is a myth. They may prove harmful when taken without supervision for qualified medical practitioners. Government and regulating agency are responsible for spreading awareness for safe use of herbal medicines [54]. Dekant et al. reported that the consumption of green herbal tea extract or infusion may responsible for hepatic toxicity in people consuming it as food supplements due to presence of catechin phytoconstitutent in infusion of herbal tea extract [55]. Thus it is advisable to take herbal supplements under the supervision of qualified medical practitioners.

4.1 Self Education

One must learn as much as possible about the herbs being taken in consultation with doctor and if need be one should not refrain from contacting herbal supplement manufacturers for information. When using herbal supplements, one must follow label instructions carefully and use the prescribed dosage only. It is recommended not to exceed the recommended dosage, and seek out information about who should not take the supplement [56]. Different scientific databases are available for whole information on single plant but at times may not be accessible due to intellectual property rights concerns. Plant information can be accessed through different sources like, CSIR database commonly known Traditional knowledge Digital Library (TKDL), MICROMEDEX (www.micormedex.com) and CRISP (www.crisp.cit.nih.gov) [12].

4.2 Follow instruction properly

Patients should exercise precautions when taking herbal drugs with conventional medicines. All label instruction points should be religiously followed before taking herbal medicine. Problems may arises during concomitant use of herbal and conventional drugs. One such example is the use of *Liquorice* with spironolactone where antagonism of diuretic effect can occur. Similarly, when *Ginseng* is taken with insulin in diabetic condition, it may change the glucose concentration and these herbs should not be prescribed in hyperglycaemic patients [57].

4.3 Professional advice

One must seek out the services of a trained and licensed herbalist or naturopathic doctor who has extensive training in this area. Such professional advice is very important in case of anticancer herbal medicines. For

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(5), 430-438 | ISSN:2251-6727

example, herbal-drug interaction between *Allium sativum* and paclitaxel may produce excessive bleeding due to bone marrow depression action [58]. Additionally, many herbal medicines have not been studied rigorously enough to verify their safety for pregnant and lactating mothers. Frawley et al. reported that the self medication with herbal drugs by pregnant women may lead to varicose vein problems. Use of herbal medicine in pregnancy case specifically in rural area has required continuous monitoring by health care providers [59]. Further monitoring is also warranted in herbal drugs used for children and infant since they may have low immunity and extensive calculations vis-à-vis dose per kg body weight and differences of metabolic enzymes may be required [60]. Thus pregnant or lactating mothers should seek help of healthcare provider prior to taking any herbal medicines to ensure the best possible outcomes [61].

4.4 Vigilance for side effects

It is essential that both the patients and the health care providers continuously watch for side effects during treatment and for adverse effects after treatment with herbal medicines. If symptoms, such as nausea, dizziness, headache, or upset stomach, occur, reduce the dosage or stop taking the herbal supplement. One must be alert for allergic reactions. A severe allergic reaction can cause troubled breathing. Different pharmacovigilance tools exist for herbal drugs safety by government agencies, like prescription event monitoring and digital database management for herbal records [62]. The World Health Organization (WHO) in collaboration with International Monitoring Programme Centre in Sweden, the Uppsala Monitoring Centre is responsible for safety vigilance of herbal drugs uses and maintains the data known as global WHO database of adverse drug reaction report. The database is continuously evolving with continuing evaluating of herbal drug uses [63].

CONCLUSION

The benefits and safety of herbal drugs cannot be undermined. With each passing day, more and more reports of drugs originating from herbal origin are pouring in. The ethno pharmacological basis of drug development is gaining further momentum due to improved extraction and isolation techniques. This chapter has tried to present a commentary on the safety and cost effectiveness of herbal drugs by providing specific examples of herb drug interactions, comparing the costs of herbal and conventional or allopathic medicines. An attempt has also been made to record reasons for toxic effects of natural herbs and the precautions one must take while taking herbal drugs or supplements. Overall, the chapter should provide a one stop solution for the prospective reader to explore different aspects related to the safety, efficacy and cost effectiveness of herbal medicines.

References

1. Li, F. S., and Weng, J. K. (2017). Demystifying traditional herbal medicine with modern approach. Nature plants, 3(8), 1-7.
2. Weng, J. K., Philippe, R. N., and Noel, J. P. (2012). The rise of chemodiversity in plants. Science, 336(6089), 1667-1670.
3. Lietava, J. (1992). Medicinal plants in a Middle Paleolithic grave Shanidar IV? Journal of Ethnopharmacology, 35(3), 263-266.
4. Patridge, E., Gareiss, P., Kinch, M. S., and Hoyer, D. (2016). An analysis of FDAapproved drugs: natural products and their derivatives. Drug Discovery Today, 21(2), 204-207.
5. Kiyohara, H., Matsumoto, T., and Yamada, H. (2004). Combination effects of herbs in a multi-herbal formula: expression of Juzen-taiho-to's immuno-modulatory activity on the intestinal immune system. Evidence-Based Complementary and Alternative Medicine, 1(1), 83-91.
6. Tyler, V. E. (1994). Herbs of choice: the therapeutic use of phytomedicinals. Pharmaceutical Products Press (imprint of Haworth Press, Inc.).
7. De Smet, P. A. (1997). The role of plant-derived drugs and herbal medicines in healthcare. Drugs, 54(6), 801-840.
8. Samojlik, I., Mijatović, V., Gavarić, N., Krstin, S., and Božin, B. (2013). Consumers' attitude towards the use and safety of herbal medicines and herbal dietary supplements in Serbia. International Journal of Clinical Pharmacy, 35(5), 835-840.
9. Calixto, J. B. (2019). The role of natural products in modern drug discovery. Anais da Academia Brasileira de Ciências, 91.
10. Zhou, J., Liu, F., Jiang, W., and Hu, M. (2019). Cost-Effectiveness of Jingshu Granules Compared to Placebo for the Treatment of Patients with Cervical Radiculopathy in China: A Decision-Tree Model Based on Randomized Controlled Trial. The Journal of Alternative and Complementary Medicine, 25(12), 1183-1192.
11. Parveen, A., Parveen, B., Parveen, R., and Ahmad, S. (2015). Challenges and guidelines for clinical trial of herbal drugs. Journal of Pharmacy and Bioallied sciences, 7(4), 329.
12. Mosihuzzaman, M. (2012). Herbal medicine in healthcare-an overview. Natural Product Communications, 7(6), 1934578X1200700628.
13. Köster, I., Von Ferber, L., Ihle, P., Schubert, I., and Hauner, H. (2006). The cost burden of diabetes mellitus: the evidence from Germany-the CoDiM study. Diabetologia, 49(7), 1498-1504.

14. Tremmel, M., Gerdtham, U. G., Nilsson, P. M., and Saha, S. (2017). Economic burden of obesity: a systematic literature review. International Journal of Environmental Research and Public Health, 14(4), 435.
15. Banthin, J. S., Cunningham, P., and Bernard, D. M. (2008). Financial burden of health care, 2001–2004. Health Affairs, 27(1), 188-195.
16. Ussher, J., and Ussher, J. M. (2011). The madness of women: Myth and experience. Routledge.
17. Nisar, B., Sultan, A., and Rubab, S. L. (2018). Comparison of medicinally important natural products versus synthetic drugs-a short commentary. Nat. Prod. Chem. Res, 6(2), 308.
18. Srivastava, K. C., Bordia, A., and Verma, S. K. (1995). Curcumin, a major component of food spice turmeric (Curcuma longa) inhibits aggregation and alters eicosanoid metabolism in human blood platelets. Prostaglandins, Leukotrienes and Essential Fatty Acids, 52(4), 223-227.
19. Sherman, P. W., and Billing, J. (1999). Darwinian gastronomy: Why we use spices: Spices taste good because they are good for us. BioScience, 49(6), 453-463.
20. Rosenblum, A., Marsch, L. A., Joseph, H., and Portenoy, R. K. (2008). Opioids and the treatment of chronic pain: controversies, current status, and future directions. Experimental and Clinical Psychopharmacology, 16(5), 405.
21. Li, T., and Ahmad, M. (2015). In vivo studies: multi-disciplinary action of Digitalis purpurea Linn. extract in rabbits.
22. Zhang, D., Yang, R., Wang, S., and Dong, Z. (2014). Paclitaxel: new uses for an old drug. Drug Design, Development and Therapy, 8, 279.
23. Walach, H. (2013). Placebo effects in complementary and alternative medicine: the selfhealing response. In Placebo and Pain (pp. 189-202). Academic Press.
24. Khan, A., and Khan, S. (2003). Placebo in mood disorders: the tail that wags the dog. Current Opinion in Psychiatry, 16(1), 35-39.
25. Bodeker, G., Burford, G., and Kronenberg, F. (Eds.). (2006). Traditional, complementary and alternative medicine: policy and public health perspectives. World Scientific.
26. Kunnumakkara, A. B., Bordoloi, D., Padmavathi, G., Monisha, J., Roy, N. K., Prasad, S., and Aggarwal, B. B. (2017). Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases. British Journal of Pharmacology, 174(11), 1325-1348.
27. Singh, A., and Zhao, K. (2017). Treatment of insomnia with traditional Chinese herbal medicine. International Review of Neurobiology, 135, 97-115.
28. Mahadevan, S., and Park, Y. (2008). Multifaceted therapeutic benefits of Ginkgo biloba L.: chemistry, efficacy, safety, and uses. Journal of Food Science, 73(1), R14-R19.
29. Kuhn, M. A., and Winston, D. (2000). Herbal therapy and supplements: a scientific and traditional approach. Lippincott Williams and Wilkins.
30. Bent, S., and Ko, R. (2004). Commonly used herbal medicines in the United States: a review. The American Journal of Medicine, 116(7), 478-485.
31. Boullata, J. I., and Nace, A. M. (2000). Safety issues with herbal medicine. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 20(3), 257269.
32. Mosihuzzaman, M., and Choudhary, M. I. (2008). Protocols on safety, efficacy, standardization, and documentation of herbal medicine (IUPAC Technical Report). Pure and Applied Chemistry, 80(10), 2195-2230.
33. Ernst, E. (2002). Adulteration of Chinese herbal medicines with synthetic drugs: a systematic review. Journal of Internal Medicine, 252(2), 107-113.
34. Hussin, A. H. (2001). Adverse effects of herbs and drug-herbal interactions. Malaysian Journal of Pharmacy, 1(2), 39-44.
35. Chan, T. Y., and Critchley, J. A. (1996). Usage and adverse effects of Chinese herbal medicines. Human and Experimental Toxicology, 15(1), 5-12.
36. Vanherweghem, J.L., Tielemans, C., Abramowicz, D., Depierreux, M., Vanhaelen-Fastre,
37. R., Vanhaelen, M., Dratwa, M., Richard, C., Vandervelde, D., Verbeelen, D. and Jadoul, M. (1993). Rapidly progressive interstitial renal fibrosis in young women: association with slimming regimen including Chinese herbs. The Lancet, 341(8842), 387-391.
38. Woolf, A. (1999). Essential oil poisoning. Journal of Toxicology: Clinical Toxicology, 37(6), 721-727.
39. DeFilippis, E. M., and Desai, A. S. (2017). Treatment of hyperkalemia in heart failure. Current Heart Failure Reports, 14(4), 266-274.
40. Chan, H., Yeh, Y. Y., Billmeier, G. J., Evans, W. E., and Chan, H. (1977). Lead poisoning from ingestion of Chinese herbal medicine. Clinical Toxicology, 10(3), 273281.
41. Wallace, L. J., Boilard, S. M., Eagle, S. H., Spall, J. L., Shokralla, S., and Hajibabaei, M. (2012). DNA barcodes for everyday life: routine authentication of natural health products. Food Research International, 49(1), 446-452.
42. Ernst, E. (2000). Herb-drug interactions: potentially important but woefully underresearched. European Journal of Clinical Pharmacology, 56(8), 523-524.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2023) 13(5), 430-438 | ISSN:2251-6727

43. Kleijnen, J., and Knipschild, P. (1992). Ginkgo biloba. The Lancet, 340(8828), 11361139.
44. Chitturi, S., and Farrell, G. C. (2000). Herbal hepatotoxicity: an expanding but poorly defined problem. Journal of Gastroenterology and Hepatology, 15(10), 1093-1099.
45. Pak, E., Esrason, K. T., and Wu, V. H. (2004). Hepatotoxicity of herbal remedies: an emerging dilemma. Progress in Transplantation, 14(2), 91-96.
46. Alonso-Castro, A.J., Ruiz-Padilla, A.J., Ramírez-Morales, M.A., Alcocer-García, S.G., Ruiz-Noa, Y., Ibarra-Reynoso, L.D.R., Solorio-Alvarado, C.R., Zapata-Morales, J.R., Mendoza-Macías, C.L., Deveze-Álvarez, M.A. and Alba-Betancourt, C. (2019). Selftreatment with herbal products for weight-loss among overweight and obese subjects from central Mexico. Journal of Ethnopharmacology, 234, 21-26.
47. Raven, P. H., Evert, R. F., and Eichhorn, S. E. (2005). Biology of Plants. Macmillan.
48. Chandra, S., and Patwardhan, K. (2018). Allopathic, AYUSH and informal medical practitioners in rural India–a prescription for change. Journal of Ayurveda and Integrative Medicine, 9(2), 143-150.
49. Azaizeh, H., Fulder, S., Khalil, K., and Said, O. (2003). Ethnobotanical knowledge of local Arab practitioners in the Middle Eastern region. Fitoterapia, 74(1-2), 98-108.
50. Vlietinck, A., Pieters, L., and Apers, S. (2009). Legal requirements for the quality of herbal substances and herbal preparations for the manufacturing of herbal medicinal products in the European Union. Planta Medica, 75(07), 683-688.
51. Abdulla, N. M., Adam, B., Blair, I., and Oulhaj, A. (2019). Heavy metal content of herbal health supplement products in Dubai–UAE: a cross-sectional study. BMC Complementary and Alternative Medicine, 19(1), 1-9.
52. Mullaicharam, A. R. (2011). Counterfeit herbal medicine. International Journal of Nutrition, Pharmacology, Neurological Diseases, 1(2), 97.
53. Fatima, N., and Nayeem, N. (2016). Toxic effects as a result of herbal medicine intake. Toxicology-New Aspects to This Scientific Conundrum. London, UK: InTech Open, 193207.
54. Eichhorn, T., Greten, H. J., and Efferth, T. (2011). Self-medication with nutritional supplements and herbal over-the counter products. Natural Products and Bioprospecting, 1(2), 62-70.
55. Lynch, N., and Berry, D. (2007). Differences in perceived risks and benefits of herbal, over-the-counter conventional, and prescribed conventional, medicines, and the implications of this for the safe and effective use of herbal products. Complementary Therapies in Medicine, 15(2), 84-91.
56. Dekant, W., Fujii, K., Shibata, E., Morita, O., and Shimotoyodome, A. (2017). Safety assessment of green tea based beverages and dried green tea extracts as nutritional supplements. Toxicology Letters, 277, 104-108.
57. Shaw, D., House, I., Kolev, S., and Murray, V. (1995). Should herbal medicines be licensed? British Medical Journal, 311 (7002), 451.
58. Vickers, A., and Zollman, C. (1999). Herbal medicine. British Medical Journal, 319 (7216), 1050-1053.
59. Ben-Arye, E., Samuels, N., Goldstein, L.H., Mutafoglu, K., Omran, S., Schiff, E., Charalambous, H., Dweikat, T., Ghrayeb, I., Bar-Sela, G. and Turker, I. (2016). Potential risks associated with traditional herbal medicine use in cancer care: A study of Middle Eastern oncology health care professionals. Cancer, 122(4), 598-610.
60. Frawley, J., Adams, J., Steel, A., Broom, A., Gallois, C., and Sibbritt, D. (2015). Women's use and self-prescription of herbal medicine during pregnancy: an examination of 1,835 pregnant women. Women's Health Issues, 25(4), 396-402.
61. Tomassoni, A. J., and Simone, K. (2001). Herbal medicines for children: an illusion of safety? Current Opinion in Pediatrics, 13(2), 162-169.
62. Sim, T. F., Sherriff, J., Hattingh, H. L., Parsons, R., and Tee, L. B. (2013). The use of herbal medicines during breastfeeding: a population-based survey in Western Australia.
63. BMC Complementary and Alternative Medicine, 13(1), 1-10.
64. Barnes, J. (2003). Pharmacovigilance of herbal medicines. Drug Safety, 26(12), 829-851.
65. Shetti, S., Kumar, C. D., Sriwastava, N. K., and Sharma, I. P. (2011). Pharmacovigilance of herbal medicines: Current state and future directions. Pharmacognosy Magazine, 7(25), 69.
66. Zhang, C. S., and Zhang, D. (2021). Evidence-based Clinical Chinese Medicine: Volume 29: Cervical Radiculopathy.
67. Baldé, N. M., Youla, A., Baldé, M. D., Kaké, A., Diallo, M. M., Baldé, M. A., and Maugendre, D. (2006). Herbal medicine and treatment of diabetes in Africa: an example from Guinea. Diabetes and Metabolism, 32(2), 171-175.
68. Adinortey, M.B., Agbeko, R., Boison, D., Ekloh, W., Kuatsienu, L.E., Biney, E.E., Affum, O.O., Kwarteng, J. and Nyarko, A.K. (2019). Phytomedicines used for diabetes mellitus in Ghana: A systematic search and review of preclinical and clinical evidence. Evidence-Based Complementary and Alternative Medicine, 2019.

69. Quesenberry, C. P., Caan, B., and Jacobson, A. (1998). Obesity, health services use, and health care costs among members of a health maintenance organization. Archives of Internal Medicine, 158(5), 466-472.
70. Hyodo, I., Amano, N., Eguchi, K., Narabayashi, M., Imanishi, J., Hirai, M., Nakano, T.
71. and Takashima, S., 2005. Nationwide survey on complementary and alternative medicine in cancer patients in Japan. Journal of Clinical Oncology, 23(12), 2645-2654.
72. Chen, Y. L., Lee, C. Y., Huang, K. H., Kuan, Y. H., and Chen, M. (2015). Prescription patterns of Chinese herbal products for patients with sleep disorder and major depressive disorder in Taiwan. Journal of Ethnopharmacology, 171, 307-316.
73. Zhou, Q. H., Zhou, X. L., Xu, M. B., Jin, T. Y., Rong, P. Q., Zheng, G. Q., and Lin, Y. (2018). Suanzaoren formulae for insomnia: updated clinical evidence and possible mechanisms. Frontiers in Pharmacology, 9, 76.
74. Komuro, A. (2017). Kampo medicines for infectious diseases. Japanese Kampo Medicines for the Treatment of Common Diseases: Focus on Inflammation, 127.
75. Singh, N. K., Sharma, A., Sharma, M., Singh, R., and Katiyar, C. (2013). Estimation of naturally produced water-soluble vitamins in different asavas and arishtas using liquid chromatography. Journal of Food and Pharmaceutical Sciences, 1(3).