



E-ISSN: 2278-4136
P-ISSN: 2349-8234
JPP 2018; 7(2): 532-536
Received: 06-01-2018
Accepted: 07-02-2018

Bhawana Khare
Research Scholar, Department of
Forensic Science, SHUATS,
Allahabad, Uttar Pradesh, India

Munish Kumar Mishra
Assistant Professor, Department
of Forensic Science, SHUATS,
Allahabad, Uttar Pradesh, India

Lav Kesharwani
Assistant Professor, Department
of Forensic Science, SHUATS,
Allahabad, Uttar Pradesh, India

Screening of adulterants in herbal formulations for forensic considerations

Bhawana Khare, Munish Kumar Mishra and Lav Kesharwani

Abstract

Herbal products are becoming very popular in these days due to its lesser side effect, and ease in availability people are moving towards these products. These herbal formulations which are available in the market without a prescription and manufacturers claim them as purely herbal, may contain synthetic substances in concentrations far above the therapeutic range and may result in severe side effects or potentially fatal interactions with conventional drugs. Therefore, stronger regulations are required to control the quality of these herbal preparations, including labeling rules, licensing, and quality assurance mechanisms verify ingredients. This paper aims to review literatures related to the adulteration present in herbal drugs, different methods of their analysis and suggestions related to safety, efficacy and improvement in the quality of herbal drugs.

Keywords: Adulteration, Herbal drugs, Antidiabetic herbal medicines, slimming herbal medicines

Introduction

From a long time ago herbs were used as the treatment of a number of diseases and illness, as in ancient time people were dependent on the nature to cure their diseases and sickness and their need resulted in finding the solution of their problems directly from the nature because in ancient time people believed that nature blessed them in the form of plants and herbs and these herbs have the remedies for all health related problems. Now people again moving towards natural and herbal products because of their lesser ill effects and also the problem in health and dissatisfaction arises from the use of pharmaceuticals, these herbal remedies are gaining popularity and preferred as the next option by the patients or consumers. Due to the increase in demands of these herbal products, the purity and effectiveness of these products which are easily available in the market becomes the matter of concern. As the herbal products are increasing in demand, the problem of adulteration in herbal products is also becoming a challenge day by day. Adulteration is mainly the activity of replacing the original crude herb partially or totally with other material which has no therapeutic value or lower in the quality and these substitutions are conducted to make the financial gain by selling the inferior quality of herb. There are two ways of adulteration one is direct and the other is indirect.

Direct or intentional adulteration: This adulteration is carried out on the basis of similarity in morphological characteristics of the original herb, in this kind of adulteration different types of substances which are lower in quality and therapeutic value are used as adulterants and due to this it lacks the therapeutic value for which it is claimed. These practices are mainly used for those drugs which are overpriced and higher in demand, to make the financial profit. Many herbs are extracted in large amount to isolate the active or therapeutic ingredient and the same herb is admixed in herbal products, but that drug is devoid of medicinal active substance as it has been extracted already. Mainly volatile oils containing drugs like clove, coriander, fennel, caraway, etc. are adulterated by this method. In these days many types of intentional adulteration are existing like extinct species, morphological similarity of herbs with low cost value, including adulteration with synthetic chemical drugs to enhance their effectiveness for the claimed purpose as in anti-obesity herbal medicines, antidiabetic herbal medicines (Khazan *et al.* 2014^[10]; Kinnari *et al.* 2015^[11]) and many other types of herbal preparations are also adulterated with chemical drugs. But these types of adulteration can result in severe health problems after consuming it in the long term.

Indirect or unintentional adulteration- This type of adulteration many times occurs without the wish or knowledge of the maker or producer. Due to the lack of knowledge and the absence of proper means of evaluation, an authentic herbal medicine partially or totally free from the active ingredients may enter the market.

Correspondence
Bhawana Khare
Research Scholar, Department of
Forensic Science, SHUATS,
Allahabad, Uttar Pradesh, India

Different factors can affect the quality of herbs such as area, climate, soil sources, growing conditions, process by which they are germinated and storage conditions, etc. Sometimes the adulteration occurs due to the negligence of the person who is collecting the herb and therefore, the herbal collector should have the knowledge of the genuine plant and that part of the plant which is higher in therapeutic ingredient and the collection of herb should be done at correct time and season to achieve the highest therapeutic value from the constituents present in it. Elimination of that part of the plant which has no active ingredient will lead to avoidance of unintentional adulteration. At the time of storage deterioration of herbs leads to the deprivation of the therapeutic ingredients, metabolite production with no activity and, many times it also results in the toxic metabolite production. Many physical factors directly or indirectly are responsible for deterioration such as, moisture, presence & intensity of light, air and temperature. These physical factors can provide a favorable environment to grow bacteria, mites and molds. Because of the morphological resemblance, the genuine herbs are substituted with others and these very often sold in the market, e.g., belladonna leaves are substituted with Ailanthus leaves, dried flowers of *Carthamus tinctorius* are mixed with saffron, many other examples are also present. The main reason behind the heavy metal contamination in food chain is the environmental pollution.

Therefore reason of adulteration in the herbal products is not always the same like to gain the financial profit but to some extent it may be because of deficient knowledge of authentic source of herb, careless collection of their species, similarity in morphology and many other reasons are also present in literatures (Prakash *et al*, 2013) [16]. According to the recent medical literatures, it was concluded that cases involving herb and drug interactions are increasing in number and they are more frequent than drug-drug interactions. The herb-drug interactions may cause severe ill effects and sometimes it may prove fatal. So to handle these types of situation, it is necessary that herbs should be appropriately labeled to alert consumers of possible interactions with other drugs, and to recommend a consultation with their general practitioners. Now it is time to consider herbs as an integrated part of medical treatment, with proper regulation on safety, quality and efficacy.

Review of Literature

Yuen *et al*, (2007) [19] discussed about the pharmaceutical analogues present in non prescription slimming products. N-nitrosfenfluramine, an analogue of fenfluramine and N-desmethyl-sibutramine, an analogue of sibutramine were found in non – prescription slimming products. These analogues are having harmful effects on the consumer's health. Three patients were hospitalized because of taking slimming products which was adulterated with analogue of fenfluramine and one patient were suffered from N-desmethyl-sibutramine, an analogue of sibutramine present as adulterant in slimming product.

Geyer *et al*, (2008) [7] stated that since 1999 nutritional supplements were analyzed by mass spectrometry methods (GC/MS, LC/MS/MS) to detect the adulteration and contamination with doping substances. The study showed that nutritional supplements contained prohibited stimulants as ephedrine's, caffeine, methylenedioxymetamphetamine and sibutramine, which were not present on labels. During 2001-2002, it was found in an international study on 634 nutritional supplements procured by as many 13 countries that almost

15% of the nonhormonal nutritional supplements were contaminated with anabolic-androgenic steroids (mainly prohormones). Anabolic steroids such as metandienone, stanozolol, boldenone, dehydrochloromethyl-testosterone, oxandrolone etc, which were not mentioned on labels, have been detected in the nutritional supplement and are used for intentional adulteration of these products.

Basu *et al*, (2010) [3] conducted a study on 29 male patients who abused herbal drug medicine, which contained opium as their undeclared ingredient. Twenty one patients were addicted to a herbal medication named as "kamini-vidravan ras" which were contained 32mg of opium per 100mg of preparation, followed by the unani preparation Barshasha in this medicine 60g of bottle contained 1.67g of opium and Dr.Jagdeep's herbal medicine were having 2.5 mg of opium in it. Qualitative analysis of the substance was done by TLC and dependency on these medicines were diagnosed by ICD-10 and DSM- IV criteria by trainee psychiatrists and confirmed by consultant psychiatrists.

Mohammad *et al*, (2010) [13] presented the contribution of thin layer chromatography in the analysis of herbal products. In this paper they have discussed about the several thin layer chromatographic systems for the detection, separation and quantification of herbal products.

Poornima B *et al*, (2010) [14] discussed about the criteria, needs and types of substitution and adulteration of herbal drug which is the major problem causing a threat to the herbal drug industry and to the research on commercial natural products. This paper is mainly focuses on the substitution of the herbs and the most essential criteria for substitution is the pharmacological activity rather than morphology. Various regulatory guidelines provided by the W.H.O should be used to carefully assess the appropriate level of testing.

Sahoo *et al*, (2010) [20] reported about the need of development of an effective marker system for isolation and identification of the individual component in herbal drugs. The main aim of this study was to evaluate the technical standards in manufacturing and the regulatory guidelines of herbal drug, authenticity and purity of herbal drugs which is becoming a challenge for the manufacturers, particularly in South East Asia. For the recognition and authentication of components present in herbal drugs Marker based standards are frequently in use, but herbal medicines are the extracts of plants so the need for adoption of multi-marker system and the effect of storage conditions are important points to be considered. They concluded that India is among the leading countries with respect to the development of pharmacopoeial standards as well as modification of existing regulatory guidelines.

Vaysse *et al*, (2010) [17] presented a new application of 2D DOSY 1H NMR for the analysis of herbal medicines and dietary supplements, which are undeniable complex mixtures. They discussed about the identification of synthetic pharmaceuticals present in herbal medicines using NMR and more specifically 2D DOSY 1H NMR which is a powerful method for providing a multivariate fingerprint of a very complex mixture especially in situations where the identity of the components is not known beforehand as it permits to consider the drug preparation as a whole.

Carvalho *et al*, (2011) [4] concluded that the phytotherapeutic formulations are widely used for the treatment of obesity and some of these phytotherapeutic formulations also contains illegal synthetic pharmaceutical as an adulterant. The main adulteration cases discussed in this literature are from Brazil, USA, Europe, and Asia. They also described the role of

chromatographic and electrophoretic methods in the analysis of adulterant present in phytotherapeutic formulations.

Kumar *et al.*, (2011) ^[12] presented an analysis of herbal antidiabetic medicine, which were found adulterated with undeclared synthetic pharmaceutical named as Metformin Hydrochloride which is an oral antidiabetic drug used in the management of type -2 diabetes. For the identification of the herbal pills UV, IR and HPLC technique were used. Quantitative measurement by UV Spectroscopy states that 100mg of powder contains 93.1mg of Metformin crystals in herbal pills. Therefore, it shows the need of strict regulation on quality control of herbal medicines and also on licensing and labelling rules.

Doreen *et al.*, (2013) ^[5] reported that increased demand of herbal medicine has resulted in the rise of concerns over its quality and safety. Strict regulations and surveillance in many Asian countries have also been imposed to protect the public's health. This study focuses on screening of possible adulterants including heavy metals, prescription drugs, poisons and steroid contamination in unregistered herbal products claimed to possess desired medicinal values. These products were analyzed by using analytical techniques such as GC-MS, HPLC-PDA and AAS. The levels of Hg (≤ 0.30 mg/kg), Pb (≤ 3.41 mg/kg) and As (≤ 0.50 mg/kg) found were below the permissible limits (i.e., 0.5, 10 and 5 mg/kg, respectively), and none of the known dangerous drugs, poisons or steroids were detected. However, all samples were found to contain an undeclared synthetic PDE-5 inhibitor, sildenafil or tadalafil, in medium to extremely high doses while two samples also contained paracetamol.

Garg and Hooda, (2013) ^[6] analyzed twenty nine Indian herbal formulations comprising analgesics, anti-diabetics and slimming products were subjected for HPLC-DAD analysis followed by UV spectra comparison with the standard compound. They concluded that The HPLC-DAD conditions were successfully applied for the determination of undeclared herbal adulterants which has a scope to be adopted by the manufacturing industries. They also concluded that, need for stricter regulations to be framed and implemented by the regulatory authorities.

Prakash *et al.*, (2013) ^[16] discussed about the prevailing trends of adulteration and substitution in herbal drugs during the present and the past. They concluded from their analysis that the sometimes unaware and illiterate suppliers adulterate herbal drugs unintentionally. Main reasons for adulteration and substitution are extinction of species, confusion in nomenclature and flawed knowledge about authentic plant. Reliable methodology for correct identification, quality assurance and standardization of ayurvedic drugs is the important aspect of today and future herbal drug analysis.

Ayres and Bond, (2014) ^[2] reported about the analysis on that drugs which have been used without medical justification for their psychoactive effects. This study focuses on the substances in legal highs, and they also discussed about their legality and safety. They purchased 22 products from different internet suppliers and concluded that out of 22 products 95% did not list the active ingredients, 23% did not contain the same ingredient as shown on website or package and 2 products were found to contain banned substituted cathinones 4-methylethcathinone (4MEC) and 4-Methylmethcathinone (4-MMC). The analytical techniques applied for each products were FTIR soectroscopy, Raman Spectroscopy and Proton Nuclear Magnetic Resonance.

Hammadi and ALmardini (2014) ^[8] proposed a simple and accurate HPLC-UV method for the separation, identification

and quantification of slimming pharmaceutical preparations such as caffeine, furosemide, phenolphthalein, sibutramine, fluoxetine and orlistat present as adulterants in natural slimming dietary supplements. They evaluated from their study that by the use of this method in less than 13 minutes six weight loss drugs have been screened which were present as adulterant in natural slimming formulation. They concluded that the mobile phase was easy to prepare with little or no variation and was economical. The time consumed in analysis was also less So this method is very convenient in the detection of any of these six adulterant present in dietary supplement or herbal preparations.

Khazan *et al.* (2014) ^[10] studied about the adulteration in herbal weight loss drugs sold in Iran markets and determined those constituents which were not mentioned in the labels of drugs on The analysis showed that six herbal products were detected with Sibutramine, three with phenolphthalein, five with bumetanide and only two herbal products detected with phenytoin. The samples were analyzed by using GC-MS and LC-MS.

Verma and Paraidathathu, (2014) ^[18] discussed about the thirty medicinal plants and their biological sources, anti - obesity active principles and their pharmacological test results. They concluded that Indian and other herbs are available in large amount in the local markets, but no herb is present that can act as a fat cutter in a very short period of time. So there is a need of awareness about the use of herbal medicine and how these medicines work for the weight reduction.

Aher and Jain, (2015) ^[1] presented HPTLC method which is simple and sensitive presence. The method was applied for the determination of adulterant and quantification of Gliclazide in its single component tablet formulations. Silica Gel 60 F254 TLC plate was used as stationary phase and Toluene: Chloroform: methanol (4:4:2 v/v) as mobile phase. Gliclazide in methanol was scanned by Camag TLC scanner 4 with UV visible detector over wavelength range 200 to 400 nm. Gliclazide showed Rf value 0.35 and scanned at 230 nm using Camag TLC Scanner. They concluded from the experiments that this method was accurate, precise and consistent for the determination and quantitative analysis of Gliclazide in tablet dosage form. Their method was validated in line with ICH guideline Q2 (R1). They reported that their method is useful in the pharmaceutical industry as their method is reliable, simple and determines the quantitative presence of Gliclazide in bulk and pharmaceutical dosage forms.

Kinnari *et al.*, (2015) ^[11] developed a HPTLC method and validated for the estimation of Glimepiride and Metformin hydrochloride. TLC aluminium plates precoated with silica gel 60F254 were used as the stationary phase and 0.5% Ammonium Sulfate: Methanol (7.5:2.5 v/v) as mobile phase. Densitometric analysis of Glimepiride and Metformin hydrochloride was carried out in the absorbance mode at 228 nm. This method gave the rf values 0.73 and 0.45 for Glimepiride and Metformin hydrochloride respectively. This HPTLC method was successfully used in the forced degradation study of Glimepiride and Metformin hydrochloride.

Popescu and Radu, (2015) ^[15] detected that active pharmaceutical ingredients present in herbal slimming food supplements and these pharmaceutical ingredients are sibutramine and fluoxetine. These substances were not declared on the label of food supplements medicines and the unawareness about the consumption of these medicines can

lead to the serious ill effects on the consumer's health. FTIR and GCMS techniques were used for the analysis of 10 dietary supplements and out of 10 samples 3 were found adulterated with sibutramine and fluoxetine.

Hayun *et al.*, (2016) [9] discussed a new, alternative, simpler, lower operating cost and validated TLC-densitometric method for screening and quantitation of sibutramine in herbal slimming drugs present in the market of Indonesia. They concluded from the analysis that six out of seven samples were containing sibutramine HCl.

Discussion

The results from the present study emphasized that there is an urgent need for quality control of herbal formulations by implementing strict regulatory guidelines by the government to ensure proper safety and efficacy. To overcome these problems stronger regulations on the control of traditional herbal medicines are required, including licensing, labeling rules and quality control mechanisms to verify ingredients need of awareness about the adulteration of herbal drugs this analysis is taken into consideration.

Conclusion

The conclusion of present study is that, herbal medicines or formulations becoming more popular day by day and easily available in the market, the content of these products are believed to be completely herbal may contain synthetic pharmaceutical substances as unclaimed ingredient and if the concentration of that substance is far above the therapeutic range then it may lead to the serious ill effects and may result in fatal interactions with conventional drugs. So it is essential that strong regulations activated for the quality control mechanisms of herbal medicines, including licensing and labeling rules to verify ingredients. When the patient is experiencing intoxication or other ill effects due to the contamination of herbal drug and doctor taking the past record of a patient then the doctor should ask precisely about drugs, dietary supplements, and so-called lifestyle products that were used without a prescription. Then it would be desirable for the contents of all such products to be declared, as required by law. When drug substances undeclared on the label which are hidden in herbal food supplements, they are dangerous for a consumer's health. Pharmaceutical substances may get involved in the consumer's diet causing adverse reactions and side effects, as the consumers are not warned about the presumptive risks of the so called "natural" product consuming.

References

- Aher A, Jain JK. Development and Validation of HPTLC Method for Determination OF Gliclazide IN API AND Pharmaceutical Dosage Form, World Journal of Pharmacy and Pharmaceutical Sciences. 2015; 4(9):1485-1493.
- Ayres TC, Bond JW. A chemical analysis examining the pharmacology of novel psychoactive substances freely available over the internet and their impact on public (ill) health. Legal highs or illegal highs? BMJ Open accessible medical research., 2012.
- Basu D, Gaur N, Das PP, Mattoo SK. Herbal medicines: Perfect Grab for Opioid Abuse? A Case Series from India. The American Journal On Addictions, 2010; 20:174-175.
- Carvalho LM, Martini M, Moreira APL, Lima APS, Correia D, Falcao T, *et al.* Presence of synthetic pharmaceuticals as adulterants in slimming phytotherapeutic formulations and their analytical determination. Forensic Science International. 2011; 204:6-12.
- Doreen NB, Chandra S, Choon-Sheen L, Mas RHM. Screening of adulterants in unregistered herbal products in Malaysia, Der Pharma Chemica, Herbal medicines in the south. 2013; 5:278-285.
- Garg M, Hooda M. HPLC-DAD Estimation of Undeclared Synthetic Compounds in selected Indian Herbal Formulations. Asian Journal of Pharmaceutical Research and Development. 2013; 1:50-54.
- Geyer H, Parr Koehler K, Mareck U, Schanzer W, Thevis M. Nutritional supplements cross-contaminated and faked with doping substances.. Journal of mass spectrometry, 2008.
- Hammadi, ALmardini MA. A Fully Validated HPLC-UV method for Quantitative and Qualitative Determination of Six Adulterant Drugs in Natural Slimming Dietary Supplements. International Journal of Pharmaceutical Sciences Review and Research; Article No. 2014; 33:171-174.
- Hayun Baitha P. Maggadani, and Amalina,N. Determination OF Sibutramine Adulterated In Herbal Slimming Products Using TLC Densitometric Method", Indonesian J. Pharm. 2016; 27(1):15-21.
- Khazan M, Hedayati M, Kobarfard F, Askari S, Azizi F. Identification and Determination of Synthetic Pharmaceuticals as Adulterants in Eight Common Herbal Weight Loss Supplements. Iran Red Crescent Med J. 2014.
- Kinnari K, Patel VV, Karkhanis, Gajjar SS. Development And Validation OF Stability Indicating HPTLC Method For Estimation OF Glimepiride And Metformin Hydrochloride", International Journal of Pharmaceutical Sciences and Research. 2015; 6:1222-1229.
- Kumar M, Mandal V, Hemalatha S. Detection of metformin hydrochloride in traditionally used Indian herbal drug for antidiabetic: A case report, International Journal of Pharma and Bio sciences, 2011; 2(2):307-312.
- Mohammad A, Bhawani SA, Shrama S. Analysis of Herbal Products by Thin-layer Chromatography: A Review", International Journal of Pharma and Bio Sciences, 2010, 1(2).
- Poornima B. Adulteration and Substitution in Herbal Drugs A Critical Analysis", International journal of Research in Ayurveda & Pharmacy. 2010; 1(1):8-12.
- Popescu AM, Radu GL. Detection of adulterants by FTIR and GC-MS in herbal slimming food supplements. Universitatea Politehnica Bucuresti Scientific Bulletin, Series B. 2015; 77(4):221-230.
- Prakash O, Jyoti Kumar A, Kumar P, Manna KN. Adulteration and Substitution in Indian Medicinal Plants", Journal of Medicinal Plants Studies. 2013; 1(4):127-132.
- Vaysse J, Stéphane Véronique G, Denis D, Malet-Martino M, Martino R. Analysis of Adulterated Herbal Medicines and Dietary Supplements Marketed for Weight Loss by DOSY 1H NMR. Journal of Food Additives and Contaminants. 2010; 27(07): 903-916.
- Verma RK, Paraidathathu T. Herbal medicines used in the traditional Indian medicinal system as a therapeutic treatment option for overweight and obesity management: A review. International Journal of and Pharmacy Pharmaceutical Sciences. 2014; 6:40-47.

19. Yuen Lai Poon, SW Ng, Albert C, Tony WLM. Adulteration of over-the-counter slimming products with pharmaceutical analogues—an emerging threat. *Hong Kong Med J.* 2007; 13(3):13:216-20.
20. Sahoo N, Manchikanti P. Herbal drug regulation and commercialization: An Indian Industry Perspective. *The Journal of Alternative and Complementary Medicine.* 2010; 19:957–963.