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Review Article

PHARMACOVIGILANCE FOR NON-POISONOUS HERBAL DRUGS

Sunitha M P[1]*, Akshatha M[2], Nischal P[2]

*[1]Associate Professor, [2]Assistant Professor, Department of Dravyaguna Vijnana, Sushrutha Ayurvedic Medical College & Hospital, Bengaluru.

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ABSTRACT

Background: An increased importance for the pharmacovigilance of herbal medicines is seen in current times because of the growing demand for the herbal products and herbal medicines globally.

Design: This involves an in-depth study of pharmacovigilance of herbal drugs from the sources such as PubMed, Google Scholar, websites etc. and also classical Ayurvedic *Granthas* like *Charaka Samhita*, *Sushrutha Samhita*, *Ashtanga Hridaya* and *Dravyaguna Vijnana* etc

Observations: Knowledge of *Aushadha Dravya* with respect to its *Nama* (nomenclature), *Rupa* (morphology), *Guna* (qualities of the drug) includes all the factors that prevents adverse drug reactions.

Conclusion: The integration including classical methods of safety assessment tools and modern technology together if adopted, the general notion of public i.e., herbal drugs are safe can be made true. Thus, even a poisonous drug can be used in therapeutics just like ambrosia for a specific diseased condition without any adverse effect as told in Ayurveda.

INTRODUCTION

The concept of pharmacovigilance is not a new topic in Ayurveda, as the very definition of Ayurveda says- It is the science which deals with the properties and actions of *Dravyas* (substances) which are having *Ayushya* (conducive for life) *Karma* and *Anayushya* (non-conducive for health) *karma*.[1]

These *Anayushkara Dravyas* are the ones which have adverse effects on the body. But such adverse effects are not universal; it varies based on various factors like i) Factors related to *Dravya- Desha* (habitat), *Kala* (time of collection) etc, ii) Factors related to *Rogi- Prakruti* (body constituent), *Vayaha* (age), etc and iii) Factors related to *Roga- Dosha*, *Dushya* etc. Thus, stating their improper usage. Hence all of these are to be considered before the administration of any drug. Otherwise even a best drug will act as *Visha* (poison). [2]

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Likewise, complete knowledge of the herb and with its judicious application, even a *Visha Dravya* (poisonous drug) can become a lifesaving drug like *Amruta* (ambrosia).

As there are not many studies on pharmacovigilance of the herbal drugs, the present study was planned to analyze the prevention of Adverse Drug Reactions (ADRs) by a detailed evaluation of both modern and ancient methods such as *DravyaPareeksha Vidhi* and *Dravya Sangrahana Vidhi*, application of *Paradi Guna* in *Chikitsa* as per our classical texts. The present study is aimed at analyzing the factors related to herbal raw materials which are likely to cause ADRs in herbal drugs and presumed to be safe drugs. The study also focuses on reviewing the traditional classical references or methods to avoid the factors which may cause adverse drug reactions.

Methodology

This study involved the search of various databases like PubMed, Google Scholar, and other scholarly research articles, classical texts of Ayurveda like *Brihatrayi* and textbooks of *Dravyaguna Vijnana*. It also includes analysis and interpretation of data.

Adverse Reactions of Herbal Drugs

Adverse events with respect to herbal products are frequent either because of poor quality or improper usage. The quality of such products depends on the:

- Good Agricultural and Collection Practices (GACP),
- Habitat
- Good storage practices for pharmaceuticals.
- Quality control methods for medicinal plant materials

Good Agricultural and Collection Practices

Agricultural Practices: For herbal raw materials there are two basic sources; collection from the wild and cultivation. With respect to this, when drugs are collected from the wild, the incidence of adulterations, use of a different botanical species of medicinal plants are very common that may lead to adverse effects. Eg: A company manufacturing a formulation containing *Senna alexandrina* Miller, terms it as Cassia in the label. Another company also manufacturing a formulation that lists "Cassia" as active ingredient but the botanical source of it being *Senna armata* Wats, a different botanical species. Reporting of serious ADRs associated with "Cassia" appears and that are serious that withdrawal of "Cassia" from the market is considered. It could be that only *Senna armata* Wats is causing these problems. In case of other species *Senna alexandrina* Miller, due to the lack of distinction between the labelled names; "Cassia" the risks are being wrongly accused. [3]

Collection Practices: Harvesting at the ideal time is crucial for the quality development after harvest and for attaining the longest postharvest life. Eg: Harvesting of banana and mangoes at the mature green stage hastens their ripening by lowering their response threshold to endogenous ethylene concentration. Bananas, therefore, can be harvested at the mature green stage and ripened later. Papaya and pineapple, however, should be harvested when partially ripe to attain good eating quality when ripe.[4]

In Ayurveda, it is specifically mentioned that *Kapittha* fruit should be used when it is completely ripened as unripe *Kapittha* causes throat problems as an adverse effect though *Kapittha* is a non-poisonous drug. The changes in the action of the drug may be because of the phytochemical changes which occur during the fruit ripening process. The study suggests as the *Feronia elephantanum* ripens, the total sugar level increases and acidic content decreases. Thus these chemical changes alters the therapeutic activity of the drug.[5] Similarly *Bilwa* fruit should be used only when it is unripe to get the therapeutic benefits.

Habitat: With respect to cultivation, growing plants in areas contaminated with toxic heavy metals, disease causing microbes, use of polluted water, soil polluted with chemicals and other potentially hazardous substances may become the cause for ADRs. Anthropogenic contaminants include the use of manures, sewage sludge, fertilisers and pesticides to soil. The consumption of plants grown in such an environment can deplete some essential nutrients in the body, decrease immunological defenses, cause intrauterine growth retardation, impaired psycho – social facilities, disabilities associated with malnutrition and high risk of upper gastro intestinal cancer occurrence.[6,7] The toxic contaminants can cause acute and chronic diseases in the human body, such as lung cancer, renal dysfunction, osteoporosis, and cardiac failure etc[8]. Contamination through parasites like amoeba, Helminths- nematode may contaminate the raw material through soil, excreta, organic cultivation etc. Some research works shown some of the pathogens like Escherichia coli, Listeria monocytogenes and Salmonella spp were isolated from animal faeces including poultry and cattle[9,10]. Some research suggests that E.coli O_{157}:H_7 can transmit to lettuce through the soil and irrigation water and can persist throughout the plant life cycle and further can transmit to those who consume those plants[11], here simple vegetable like lettuce, though it's a common non-poisonous plant regularly used as a vegetable, may cause ADRs, not because of the drug but due to the other factors like improper cultivation, habitat in this case.

Post-Harvest Processing, Storage: According to WHO, during the post-harvest processing, transportation and storage, mycotoxins, biological toxins like bacterial endotoxins may contaminate the raw material. Similarly, bacterial contaminations like Staphylococcus aureus, Salmonella sp, E.coli, during harvest, processing, transportation and storage. Contamination by insects like Cockroaches and its parts, mouse excreta may contaminate during post – harvest processing, transportation and storage. [12]

Quality Control Methods: The chances of adulteration can be reduced by subjecting the given drug to quality control studies like foreign matter, organoleptic characters, pharmacognostic characters, macroscopic and microscopic, physicochemical, phytochemical parameters etc. Usage of specific species of plant source, potency of the drug used can also be identified. These can significantly check ADRs[13].

Ayurvedic Guidelines to Overcome ADRs: In Ayurveda it is clearly mentioned that if a person is not having good knowledge of the *Aushada Dravya* with respect to its *Nama* (name), *Rupa* (morphology/ pharmacognostic features), *Guna* (properties and actions) or inspite of having knowledge of these three but if it is utilized improperly in therapeutics it will

lead to *Anartha* (adverse effect) [14]. This covers most of the guidelines to avoid adverse drug reaction.

Apart from that, in *Dravyaguna shastra*, *Dravyasangrahana* is explained in detail like *Prashasta Desha* (habitat). The altitude, annual sunshine duration and annual mean temperature plays an important role in the production of optimal quantity of phytoconstituents.[15] *Prashasta Bhumi* (soil type depending on the plant) - Because quality of the soil is responsible for the ideal quantity of the phytochemical constituents of the plants[16]. *Sangraha Kala* (season of collection)- Season and time of collection of drug determines the presence of functional groups in optimal level Eg: *Ashwagandha* collected in the *Greeshma Jyeshta Paurnima* (GJP) and *Asadha Pournima* (GAP) samples were found to be superior than *Amavasya* samples w.r.t functional groups and with anoloid content respectively on HPTLC[17]. *Sangraha Vidhi* (method of collection/harvesting)- Good collection practice or sustainable harvesting ensures the quality of the raw materials which in turn improve the safety and efficacy of the finished products[18]. One should take care while collecting the herbal drug that no foreign matter, weed or toxic plant get admixed with the raw material, which may become the cause for the adverse effect. [19]. *Samskara* (post harvesting processing)- If the raw material is not stored scientifically, especially in tropical and subtropical countries like India due to the high temperature and moisture which is ideal for the growth of fungus and mycotoxins results in the contamination with fungus and mycotoxins. The most common mycotoxins reported on stored herbal drug raw materials are aflatoxins, ochratoxin, citrinin and fusarium spp., respectively. The fungus apart from having toxic effects also deteriorates the quality of the raw drug when it interacts with the raw material. The fungi absorbs the nutrients from the raw materials by secreting hydrolytic enzyme which changes the complex active compounds of the raw materials into simple ones but useless or less efficacious forms of the chemicals, thus degrades the quality of the drug as well. [20]

Acharya Sushrutha explains the characteristics the drugs should possess for collection as mentioned below: *Krimianupahata* (not infested), *Vishaanupahata* (not affected by toxins), *Shastra anupahata* (not affected by weapons), *Atapaanupahata* (not affected by extreme heat), *Pavanaanupahata* (not affected by wind/ storm), *Dahanaanupahata* (not affected by fire), *Toya anupahata* (not affected by water/ moisture), *Sambadhaanupahata* (not affected by other problems), *Margaanupahata* (not destroyed/damaged by rampage), *Ekarasam* (*Utkrushta rasa* – best quality), *Pushta* (well grown and nourished), *Pruthu* (*Pruthu Valkala*- Plant should possess abundant bark), *Avagada Moola* (deep rooted). Such plants only should be collected[21]. If this is not followed, it will become the root cause for anthropogenic contamination, thus leading to ADRs.

Along with *Acharya Sushrutha's* reference, *Acharya Charaka* has elaborately explained about the *Dravya-Pareeksha Vidhi* in *Vimanasthana* 8th chapter[22], which is very similar to the present day monographs of drug. According to this, a drug should be studied as follows:

1. ***Prakruti*:** Name, natural order and morphology. So that the specific species of the drug can be used. The fact that most medicinal plants used by the traditional practitioners and manufacturers of Ayurvedic products are collected from the wild have problems for identification and obtaining material of uniform quality due to a number of reasons. Sometimes a plant name may refer to more than one species: the name *Brahmi* can refer to either *Bacopa monneiri* or *Centella asiatica*, which have entirely different phyto-chemical compositions. *Shankhapushpi* is one of the *Rasayana* drugs in Ayurveda and several plant species are being reported as *Shankhapushpi*, viz. *Convolvulu spluricaulis, Clitoria ternatea, Evolvulus alsinoides* and *Tephrosia purpurea* in different regions in India[23].
2. ***Guna*:** It includes *Rasa*, *Guna*, *Veerya*- the chemical properties of the drug. If a drug possesses the properties as mentioned in the classics, then it will ensure the safety as well as the efficacy of the drug. To achieve all the properties of the drug, a drug must be collected at proper stage of maturation. A study conducted by Pandey and Mandal (2010) revealed that the maximum amount of andrographolide (2.85%) was found in a *A.paniculata* when harvested after 130 – 150 days of planting (at the time of initiation of flowering) [24].
3. ***Prabhava*:** The actions of the drug.
4. ***Desha*:** Habitat of the drug- The drug collected from the ideal place will have the desired active principles and will not have any adverse effects.
5. ***Rutu Gruheetam*:** Time and method of collection- Drugs collected at proper time will ensure the qualitative and quantitative standards of the phytochemical constituents. *Adhatodavasica* is a bronchodilator drug of Ayurveda. The plant shows wide seasonal variation in vasicine content in its leaves. It exhibited higher levels of vasicine twice in a year i.e., 3.0% in March and 1.4% in September. Interestingly, it coincided with the flowering of the plant. In March, it was full bloom condition and in September, it was partial flowering. During the vegetative stage, the plant contained very low

concentration of vasicine[25]. The concentration of alkaloid in the roots of *Rauvolfia serpentine* is highest at after 18 months of planting in the month of December[26].

6. ***Nihita*:** Method of preservation- Proper storage of the raw material keeps the drug unaltered and will not have any toxin formation. After collection, the raw material should be stored in a clean containers and in a proper way, i.e., overfilling or stacking of sack or bags may cause composting and formation of moulds thus releasing the toxins[27].
7. ***Upaskrita*:** *Samskara*- Processing of the drug and its formulations- Primary processing after the harvest like drying and washing should be done properly otherwise increases the foreign matter content in the raw material. Improper drying process because of high ambient air temperature and relative air humidity during the season of harvesting supports the formation of insects and moulds in the harvested crop thus increasing the microbial load in the raw material. This microbial contamination may become cause for some adverse effects.
8. ***Matra*:** Dosage- Drugs prescribed in proper dosage, will show the specific therapeutic effect without any Adverse event even if the *Vishadravya* is used (*Shodhita*- after purification).
9. ***Vyadhi*:** Different conditions where the drug can be therapeutically used. Prescribing a drug after proper diagnosis of the disease and assessing the stage of the disease (*Vyadhiavasta*) can prevent the adverse effect. Eg: In *Amatisara Deepana, Pachan* and *Grahidravyas* should be prescribed whereas in *Pakwatisarastambhana dravyas* should be prescribed, if *Stambhanadravyas* like *Kutaja* etc is given in *Amatisara* even though *Kutaja* is a non-poisonous drug, in that condition it may show some ADRs, where the ADRs is not because of the drug, it is because of the improper assessment of the *Vyadhiavastha*[28].
10. ***Evam vidhapurushasya*:** Clinical trials or in which person it is probably useful. Prescribing the drug after assessing an individual completely with respect to *Prakruti, Vaya* etc will not show any adverse effects. Eg: Though *Hareetaki* is a *Rasayana Dravya* having synonym as *Amruta*, it is contraindicated in *Bala*, *Vruddha*, *Garbhini* etc, hence a drug should be prescribed after assessing the condition of an individual, thus a person will not end up with any adverse effects.

    If all these ten factors are stringently considered while administering the drug ADRs due to *Dravya*, *Rogi* and *Roga* related factors can be avoided.

Application of *Paradi Gunas*: *Acharya Charaka* explains about ten special *Gunas* which are useful for treatment, called as *Paradi Gunas*. They are

1. ***Paratwa*:** That which is conducive for health. Again, this conduciveness depends on *Desha* - Plant habitat plays an important role with respect to the quantity of the active principles. Eg: The phyto-components of liquorice showed variation based on different geographical locations of Iran. It was observed that the amount of glycyrrhizic acid was maximum in Bajgah (74.00mg/g dry weight) and minimum in Taft (13.43mg/g dry weight) populations. However, glabridin content was found to be highest in Kashmar popupation (12.88mg/g dry weight). Also, the greatest antioxidant activity (the lowest IC_{50}) for liquorice root which is 44.4, 56.5 and 59.5 µg/ml was associated to Kashmar, Meshkinshahr and Eghlid populatios with IC_{50} equal to respectively. Moreover the antioxidant activity in a methanolic extract of aerial part was remarkable in Kazerun, Taft and Ahar populations. Consequently, frequency ration (FR) model was run to map the habitat suitability of *Glycyrrhiza glabra* based on annual average temperature, average yearly precipitation and altitude[29]. *Kala- Dravya Sangraha Kala* (season of collection of drugs) as told in the classic is said to be para and collecting the same drug in other than the prescribed season is said to be *Apara*. *Vaya*: Some of the drugs like *Hareetaki* is contraindicated in *Bala*, hence it is *Apara*- Non conducive in children based on *Vayah* whereas the same *Hareetaki* is said to be *Rasayana* in others thus a drug based on the age of the patient may act like a medicine or the same may become cause for some untoward effect though it is a non poisonous drug like *Hareetaki*. *Mana*: Quantity- dosage etc of the prescribed drug. Drugs like *Yashtimadhu* are proven to be *Vamanopaga* i.e., assist in the vomiting therapy at the same time it is also said to be Antiemetic. *Yashtimadhu* contains carbenoxolone derived from glycyrrhetinic acid, and it is reported that carbenoxolone can increase mucous production, which can inhibit vagus irritation in the gastrointestinal tract and accelerate the antiemetic effect[30]. In large dose the same *Yashtimadhu* acts as emetic[31].
2. ***Aparatwa*:** The factors which are non-conducive to health. They vary again according to *Desha*, *Kala* etc. such things should be withdrawn otherwise may aggravate the condition.
3. ***Yukti*:** *Acharya Charaka* says, that all *Dravyas* in this universe can be used as a medicine if it used in accordance to *Yukti* (logical reasoning), Even in *Bhavaprakasha Nighantu* it has been clearly mentioned that, if a physician feels any particular drug is not suitable to an individual even though it is mentioned in the classics, can be removed from the formula. Similarly, if any drug a physician feels

suitable to a person even though not mentioned in the classics can be included thus one can get the beneficial effects without any adverse effect[32]. A physician can use his *Yukti* and decide which *Samskara* can decrease the adverse effects of the drugs and which will enhance the efficacy of the drug[33].

4. ***Samkhya*:** Counting or calculation is very important to decide the dosage, its frequency and duration. Otherwise, it may lead to dose related toxicity, cumulative effect due to long term usage etc even though a drug is non-poisonous. Often patient may be taking acute or chronic overdose, which may cause medium- or long-term toxicity without proper knowledge, where the toxicity or adverse effect is not due to drug, because of wrong dosage and duration of treatment. [34]
5. ***Samyoga*:** Combination of different drugs to act synergistically as well as to avoid adverse effect. Drugs when combine with other drug can act antagonistically and reduce the toxicity or intensity of the drug. Eg: Presence of antidotes in the formulation containing *Visha Dravyas* or they may act synergistically with each other and enhance the potency of the drug. Eg: *Anupana* to increase the action of the drug or for its quicker action and adding antidotes in formulations containing *Visha Dravyas* to reduce the adverse effect form.
6. ***Vibhaga*:** Preparation of different dosage forms like *Grita, Taila, Kashaya* etc isolating the alcohol soluble, water- soluble principles only from any drug. The quantity of active principles in different drugs varies according to the media/solvent used. Eg: *Arjuna* yields more extract value when used ethanol compared to other solvents like acetone, water or chloroform, which substantiates the use of *Arjuna* in the form of *Arishta* rather than *Kashaya.* Thus we are isolating (*Vibhaga*) the more quantity as well as a specific extracts which are soluble in alcohol[35].
7. ***Prutaktwa*:** Unique characteristics of the drugs.
8. ***Parimana*:** Quality which aids in measurement, while explaining the *Grahya Dravyas*, specific measurements are explained for Eg: Features of ideal *Hareetaki* is explained as that which is pulpy, having a small seed, which is heavy, having 2 *Karshapramana* and sinks in water is considered as ideal one and produce the desired effect, otherwise it may have some other pharmacological action[36,37]. Eg: *Bala Hareetaki*- Unripen fruits of *Hareetaki* which usually does not possess seeds possess different pharmacological action than the *Hareetaki*. Thus, stating the importance of the organoleptic characteristics of the drugs.
9. ***Samskara*:** The factors which imparts, modifies the qualities of a substance, thus making a substance more bio-available form, reduced toxicity and adverse effects. Certain medicinal plants not categorized under poisonous drugs like *Vacha* (*Achorus calamus* Linn), *Vriddhadaru* (*Argyreia speciosa* Sweet), *Hingu* (*Ferula foetida* Bioss), *Kampillaka* (*Mallotus philippensis* (Lamk) Muell-Arg) and *Guggulu* (*Commiphora mukul* (Hook.ex. Stocks) Engl.) etc., are also recommended to pass through specific *Shodhana* process before administration. Classically *Shodita Vacha* also showed relatively better effect in case of acute as well as chronic administration compared to the raw *Vacha*. So that chronic toxicity due to long term usage can be prevented[38]. Apart from this, a physician or a consumer of a *Dravya* should know, which are the *Samskaras* which are contraindicated for specific *Dravyas*, Like for example- *Gruta, Taila, Kashaya* should not be reheated once they are prepared, otherwise they become poisonous or alike[39]. Thus a physician should know, even though these *Gritha, Taila, Kashaya* are non poisonous substances, they may act like poison and cause ADRs if administered improperly as said above.
10. ***Abhyasa*:** Regular usage of *Pathya Dravyas* and gradual withdrawal of *Apathya Dravyas*. Eg: In patients suffering from *Rajayakshma* should withdraw himself from excess of physical activity as it is one of the *Nidana* of *Rajayakshma* (*Ayathabalamarabhya*)[40], otherwise further the condition of the person deteriorates, here the worsening of the condition will not be because of the drugs, because of the *Apathya Vihara* which one should gradually withdrawn.

DISCUSSION

Thus, all the factors which are explained in *Dravya Sangrahana Vidhi*- Harvesting techniques, *Samskara Vidhi*- Post harvest processing, *Sangrahana* in *Bheshajagara*- Storage of the raw material, including *Desha*- Habitat, *Bhumi*- Soil quality, *Sangraha Kala*- Season of collection, and application of these *Dravyas* properly in patients considering the *Paradiguna* etc, will help to overcome the ADRs related to anthropogenic contaminations, adulterants, poor quality of the raw materials and improper clinical usage of the drugs, which are the cause for ADRs with respect to non poisonous herbs, not the *Dravya.*

CONCLUSION

The basic philosophy behind the data management of herbal products and traditional medicines is to achieve a system that is capable of handling all levels of information, like identification of medicinal plant, itemization of the medicinal plant part

(herbal material), stipulation of preparation methods (processing including extraction procedures/ preparations), note of any variations in product composition (and dosage form) and intended medical use, indicating diseases or symptoms that can be treated.

All these are explained in detail in above said *Dravya Pareekshavidhi*, *Dravya Sangrahana*, application of *Paradi Guna* in *Chikitsa* in our classical texts. Hence, by the integration of classical methods of safety assessment tools and modern technical methodologies together if it is adopted, the myth of common people i.e., herbal drugs are safe can be made true. Thus, even a poisonous drug can be used in therapeutics just like ambrosia for a given diseased condition without any adverse effect as told in Ayurveda.

REFERENCES

1. Charaka Samhita of Agnivesa, Chakrapani Datta's Ayurveda deepika (sans), 1st ed, Sutra Stahna, Dashamahamooliya Adhyaya, 30 / 23 Chaukhambha Sanskrit Series office, Varanasi, 2006, pp 187
2. Charaka Samhita of Agnivesa, Chakrapani Datta's Ayurveda deepika (sans), 1st ed, Sutra Stahna, Deergam jeeviteeyam adhyaayam, 1/126, Chaukhambha Sanskrit Series office, Varanasi, 2006, pp 23.
3. WHO Guidelines on safety monitoring of herbal medicines in pharmacovigilance, https://apps.who.int/iris/bitstream/handle/10665/43034/9241592214_eng.pdf
4. Postharvest technologies to maintain the quality of tropical and Sub Tropical Fruits, yahia E.M. in Postharvest Biology and Technology of Tropical and Subtropical Fruits: Fundamental Issues, 2011
5. International journal of fruit science, "Post-Harvest Ripening Changes in Wood Apple (Feronia elephantumCorr), An Underutilized Fruit" @eng, Publisher: Taylor & Francis, In AGRIS since: 2016, Volume: 15, Issue: 4
6. Iyengar GV, Nair PP (2000) Global outlook on nutrition and the environment: meeting the challenges of the next millennium. Sci Total Environ 249: 331 - 346
7. Turkdogan MK, Kilicel F, Kara K, TuncerI, Uygan I (2003) Heavy metals in soil, vegetables and fruits in the endemic upper gastrointestinal cancer region of Turkey. Environ ToxicolPharmacol 13:175-179.
8. Ying L., Shaogang L., Xiaoyang C. Assessment of heavy metal pollution and human health risk in urban soils of a coal mining city in East China. Hum. Ecol. Risk Assess. An Int. J. 2016;22:1359–1374.
9. J. Buck, R. Walcott, and L. Beuchat, Recent trends in microbiological safety of fruits and vegetables, Plant Health Progress, vol. 4, no. 1, p. 25, 2003.
10. K. Söderqvist, "Is your lunch salad safe to eat? Occurrence of bacterial pathogens and potential for pathogen growth in pre-packed ready-to-eat mixed-ingredient salads," Infection Ecology & Epidemiology, vol. 7, no. 1, Article ID 1407216, 2017.
11. A.K. Bhunia, Food borne Microbial Pathogens: Mechanisms and Pathogenesis, Springer, Berlin, Germany, 2018b
12. WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues. https://apps.who.int/iris/handle/ 10665/43510
13. Balekundri, A., Mannur, V. Quality control of the traditional herbs and herbal products: a review. Futur J Pharm Sci 6, 67 (2020). https://doi.org/10.1186/s43094-020-00091-5
14. Charaka Samhita of Agnivesa, Chakrapani Datta's Ayurveda deepika (sans), 1st ed, Sutra Stahna, Deergam jeeviteeyam adhyaayam, 1/125, Chaukhambha Sanskrit Series office, Varanasi, 2006, pp 23.
15. Liu,W., Yin,D., Li, N. et al. Influence of Environmental Factors on the Active Substance Production and Antioxidant Activity in Potentilla fruticosa L. and Its Quality Assessment. Sci Rep 6, 28591 (2016). https://doi.org/10.1038/srep28591
16. Mamatha Sandhal, Shobha G. Hiremath, Surekha Medikeri. Classical approach to collect medicinal plants-A prudent view in optimizing pharmacological affluence. J Ayurveda Integr Med Sci 2017; 4: 191-199. http://dx.doi.org/10.21760/ jaims.v2i4.9351
17. Tavhare SD, Nishteswar K, Shukla VJ. Effect of seasonal variations on the phytoconstituents of Aśvagandhāw.r. to lunar cycles. Anc Sci Life. 2016; 35(3): 150-158.
18. A.K. Pandey and Rameshwar Das, 2014. Good Field Collection Practices and Quality Evaluation of Medicinal Plants: Prospective Approach to Augment Utilization and Economic Benefits. Research Journal of Medicinal Plants, 8:1-19.DOI:10.3923/rjmp. 2014. 1.19.
19. AK Pandey and Savita, Harvesting and post-harvest processing of medicinal plants: Problems and prospects, The Pharma Innovation Journal 2017; 6(12): 229-235.
20. Dubey, N. K., Mishra, P. K., Kedia, A., & Prakash, B. (2014). Fungal and Mycotoxin Contamination of Herbal Raw Materials and Prospects of Higher Plant Products as Plant-Based Preservatives During Post-Harvest Processing. Microbial Diversity and Biotechnology in Food Security, 495–504.
21. Vaidya Jadavji Trikamji Acarya, Sushrutha Samhita of Sushrutha, Dalhanacharya's Nibandha sangraha (Sans), 1st ed, Sutra Sthana, Bhumipravibhageeyam adhyayam, 36/3, Chaukhambha Sanskrit Series office, Varanasi, 2008, pp 158.
22. Charaka Samhita (ISBN: 81-218-0062-5) of Agnivesa, Chakrapani Datta's Ayurveda deepika (sans), 1st ed,

Vimana Sthana, Rogabhishag-jiteeyam Vimana, 8/87, Chaukhambha Sanskrit Series office, Varanasi, 2006, pp 275
23. AK Pandey and Savita, Harvesting and post-harvest processing of medicinal plants: Problems and prospects, The Pharma Innovation Journal 2017; 6(12): 229-235
24. Pandey AK, Mandal AK. Variation in morphological characteristics and andrographolide content in Andrographis paniculata (Burm.f.) Nees of central India, Ira. J. En. & Env. 2010; 1(2):165-169
25. Bagchi GD, Dwivedi PD, Haider F, Singh S, Srivastava S, Chattopadhyay S. Seasonal variation in vasicine content in Adhatoda species grown under north Indian plain conditions. J. Med. Aro. Pl. Sci. 2003; 25: 37-40
26. Pandey AK, Mandal AK. Variation in morphological characteristics and andrographolide content in Andrographis paniculata (Burm.f.) Nees of central India, Ira. J. En. & Env. 2010; 1(2): 165-169
27. AK Pandey and Savita, Harvesting and post-harvest processing of medicinal plants: Problems and prospects, The Pharma Innovation Journal 2017; 6(12): 229-235
28. AvinashKarambhe, Vrinda. P. Kadu: Dehydration In Children With Reference To Atisar And Its Management With Ayurveda. International Ayurvedic Medical Journal {online} 2019 {cited December, 2019} Available from: http://www.iamj.in/posts/images/upload/2324_2327.pdf
29. Hassan Esmaeili, Akbar Karami, Javad Hadian, Mohammad Jamal Saharkhiz, Samad Nejad Ebrahimi, Variation in the phytochemical contents and antioxidant activity of Glycyrrhiza glabra populations collected in Iran, Industrial Crops and Products, Volume 137, 2019, Pages 248-259, https://doi.org/10.1016/j.indcrop.2019.05.034.
30. Mamgain Ravindra Kumar, Gupta Meenu, Mamgain Pratibha, Verma Sanjeev Kumar, Pruthi Deep Shankar, Kandwal Abhishek, Saini Sunil, The efficacy of an ayurvedic preparation of yashtimadhu (Glycyrrhiza glabra) on radiation-induced mucositis in head-and-neck cancer patients: A pilot study, Year: 2020 | Volume: 16 | Issue Number: 3, | Page: 458-462, Journal of Cancer Research and therapeutics.
31. Dunumala, B., Paheerathan, V., & Piratheep kumar, R. (2020). Evaluation of antioxidant and phytochemical analysis of water extracted root powder of Glycyrrhiza Glabra. Sri Lanka Journal of Indigenous Medicine (SLJIM), 5, 424-428
32. Dr.BulusuSitsram, Bhavaprakasha of Bhavamishra, Vol 1, Chapter – 6 (I)/ 168, Mishra prakarana, Pg.No: 117, Publisher: Chaukhamba orientalia.
33. Shriwas, H. K., Ratre, S. G., & Chandrakar, R. (2019). Yukti Pramana And Its Applied Aspect in Ayurveda: A., World Journal of Pharmaceutical Research, Volume 8, Issue 7, 621-626
34. Shaw, D., Graeme, L., Pierre, D., Elizabeth, W., & Kelvin, C. (2012). Pharmacovigilance of herbal medicine. Journal of ethnopharmacology, 140(3), 513-51
35. T.N. Padma Shree et.al; Journal of Pharmacology and Toxicology Volume 2, Number 8, 698-708, 2007.) (T.N. Padma Sree, S. Krishna Kumar, A. Senthilkumar, Gopala Krishna Aradhyam and Sathyanarayana N. Gummadi, 2007. In vitro Effect of Terminalia arjuna Bark Extract on Antioxidant Enzyme Catalase. Journal of Pharmacology and Toxicology, 2:698-708. DOI: 10.3923/jpt.2007. 698.708, URL: https://scialert.net/abstract /?doi=jpt.2007.698.708
36. Dr.Bulusu Sitaram, Bhava Prakasha of Bhava Mishra, Vol I, Chaukhambaorientalia, Purva Khanda, Hareetakyadivarga - 6/2/ 28 - 29, Pg No: 132.
37. Dr.Bulusu Sitaram, Bhava Prakasha of Bhava Mishra, Vol I, Chaukhamba orientalia, Purva Khanda, 6/1/ 113- Pg No: 112
38. Acharya, R. (2014). Shodhana: an Ayurvedic detoxification technique and its impact on certain medicinal plants. Conservation, cultivation and exploration of therapeutic potential of Medicinal plants. 1st ed. New Delhi: Central council for Research in Ayurvedic Sciences, 427-50
39. Dr.Bulusu Sitaram, Bhava Prakasha of Bhava Mishra, Vol I, Chaukhamba orientalia, Purva Khanda, 6/1/ 110 - Pg No: 112
40. Pandit Kashinath Shastri, Charaka Samhita, with Hindi vidyotini commentary, Vol 2, Ckikitsa Sthana 8/ 13, Pg No: 279, Chaukhamba Bharati Academy, Reprint: 2006

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***Address for correspondence**
Dr. Sunitha M P
Associate Professor,
Department of Dravyaguna Vijnana, Sushrutha Ayurvedic Medical College & Hospital, Bengaluru.
Email: drsunitha.mp@gmail.com