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Case Report

Moringa oleifera Lam. Enriched Biscuits Induced Adverse Drug Reaction- a Case Report

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ABSTRACT

Background: *Moringa oliefera Lam. (Shigru/Moringa) is used as day to day edible product and as well as medicinal purpose for its enriched nutrients and medicinal values. Thus the biscuits of Shigru leaves were prepared to carry out a clinical trial to correct Iron deficiency anaemia in females. Out of 51 recruited participants during the clinical trial, one case of adverse drug reaction was reported.*

Materials and Methods: *An 18 year female participant with 39 kg weight included in research trial as her Hb% was 10.2 and serum ferritin was 3.85. Moringa oliefera enriched biscuits were given in a dose two biscuits twice daily since 7 September 2019. She has reported after 5 days i.e. on 12 September 2019 with the complaint of red rash over back and arm. She was advised to withdraw the biscuits immediately got relief within 24 hours. After restarting the biscuits, she reported again rash with itching, then a case of ADR recorded and Ayurveda treatment has been initiated.* ***Result:*** *After Ayurveda medication within 12 hours she got relief from itching and red rash disappeared gradually.*

Discussion and Conclusion: *Moringa is even though commonly used as in many edible forms; the Moringa enriched biscuit reported 1 ADR out of 51 recruited participants. This is important and helpful for pharmacovigilance to record and control adversity that affects the issues of consumers and regularization of Ayurveda health care system.*

Key words: *Moringa oliefera, Shigru, Adverse drug reaction, Pharmacovigilance, Shatadhauta Ghruta, Laghusutashekhara Rasa, Avipattikara churna*

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INTRODUCTION

Adverse drug reaction (ADR) is defined as "an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product." Somebody well said that where there is action there will be reaction even. Any product that acts as medicine will have a capacity of giving reaction including Ayurveda Herbal product.

Adverse drug reactions are classified into six types (with mnemonics): dose-related (Augmented), non-dose-related (Bizarre), dose-related and time-related (Chronic), time-related (Delayed), withdrawal (End of use), and failure of therapy (Failure). Timing, the pattern of illness, the results of investigations, and rechallenge can help attribute causality to a suspected adverse drug reaction. Management includes withdrawal of the drug and possibly with specific treatment of ADR counter effects. Suspected adverse drug reactions should be reported regularly to develop counter management mechanisms and preventive measures to adopt. Surveillance methods can detect reactions and prove associations.[1]

The Ayurveda, the ancient healthcare system is practised in India since 1500 BC. Ayurveda was the first medical system considered and recorded the situations of adverse drug reactions (ADRs) and incorporated methods to avoid or nullify the ADR. The lists of drugs were classified as toxic, semi-toxic or to be used with precaution or after *shodhana* or *samskara* etc. Even in certain texts, management for possible ADRs or toxicity have been mentioned in detail. But, it is in need to prove that the drugs of these systems are safe, based upon a comprehensive safety data or based upon clinical and pharmacological studies. It is to be appreciated that, there is no drug which is devoid of toxicity and the drugs without toxicity are likely to be without any effect. Hence, what is important is to assess

the relative safety of administering an herb/drug product in a simulative situation. [2]

Pharmacovigilance plays an important role in optimizing drug safety and improving treatment outcomes. Pharmacovigilance is defined as the science and activity concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines (ADRs). The ultimate goal of this activity is to improve the safe and rational use of medicines, thereby improving patient care in public health domain. [3]

More ADR reports related to herbal medicine reported now a day. This may be due to more people attracted for the usage of herbal products either as a medicine or nutritional supplements. In some cases it is observed that people are used the herbal medicine/products without prescription and for long period. Such sensationalised and over reacted reports of media tend to spread negative perception regarding the use of herbal medicines especially Ayurveda. Such reports many a times neglect to identify the cause behind the case which can be referral to variety of issues that are considered in Ayurveda well in advance and recorded. The affirmations of Ayurveda are neglected many a times either due to ignorance or negligence by the manufactures and not followed by the consumer. Hence, implementation of Pharmacovigilance in Ayurveda is the need of the hour to address these issues and to make system more strong and scientific. [4]

Moringa oleifera Lam. is known as drumstick, *Sahjan*, *Shobhanjana* or *Shigru* in India. It is a perennial tree, belongs to *Moringaceae* family. All parts of plant are having incredible range of some functional and nutraceutical properties which make this plant full of diverse biomaterials for food and allied uses. Moringa leaves are very rich source of vitamins, minerals, protein and essential elements. High nutritional values of its edible portions pave a way in making this plant more popular as an important food source. It is also used in order to combat protein energy malnutrition problem which is prevailed in most of the under developed and developing countries of the world. Presence of various types of antioxidant compounds make this plant leaves a valuable source of natural antioxidants and a good source of nutraceuticals and functional components as well. [5]

Till now, there is lack of data regarding the nutritional supplementation using *Moringa oleifera* Lam. leaves fortified food products for treatment of anaemia. It is necessary to check and assess whether these Moringa fortified food products has any clinical significance and capable of iron bioavailability in this plant or not. The effect of food products fortified with Moringa leaf powder on haemoglobin and serum ferritin is witnessed through a research work on Iron deficiency anaemia undertaken at Mahatma Gandhi Ayurved College Hospital and Research Centre, Wardha (M.S.) with the collaboration of Forest Research centre for skill development, Chhindawad (M.P.). This presented case of ADR was found during the clinical trial of this research project.

CASE REPORT:

An 18 years female participant included in research trial as her Hb% was 10.2 and serum ferritin was 3.85. *Moringa oliefera* enriched biscuits were given in a dose two biscuits twice daily since 7 September 2019. The content of biscuits depicted in Table-1. She has reported with the complaint of rash over back and arm after 5 days i.e. on 12 September 2019. She was advised to withdraw the biscuit immediately. By the second day, the rash was minimised. The biscuit was restarted on the third day and she has started the itching with aggravated rash, then again asked to withdraw the biscuits. And a case of ADR is recorded and followed with Ayurveda treatment (Table-2).

Table 1: Details of Biscuit contents

Ingredients	Quantity
Fine wheat flour	250g
Sugar	250g
Ghee	300g
Milk powder	25g
Milk	100g
Baking powder	4g
***Moringa oleifera* leaves powder**	12.5g/kg

Table 2: ADR managed by Intervention

Date	Medicine	Contents	Dose
15/09/2019	*Laghusutashekhara rasa*	*Swarna gairika, Sunthi Nagavalli swarasa bhavana*	250 mg twice daily before meal
	Avipattikara churna	*Trikatu, Triphala, Musta, Vidalavana, Vidanga, Ela, Tejapatra, Lavanga, Nishotha, Sharkara*	20 gm at bedtime with Luke warm water for *virechana*
	Shatadhauta ghruta	*Goghruta*	for external application over rash

General Examination: General condition of participant was good. Pulse rate: 82/min, B.P. 110/80 mm of Hg, Pallor absent, Weight- 39 kg, Height- 152 cm. Red rash present over arm and back. Itching was present at rash site.

Systemic examination: RS - clinically clear, CVS – S1 S2 normal. No abnormal sound, CNS – well conscious oriented, P/A: Soft, non-tender; Liver, Kidney, Spleen-not palpable

Ashta vidhpariksha: Nadi – Pitta pradhan vata, Mala – malavshtambha (intermittently), Mutra –samyakpraritti, Jivha – sama, Shabda – spashta, Sparsh – anushana, Druk –prakruta, Akriti – alpa (thin built).

Stroto dushti: raktavaha Strotas: twacha dushti (rakta varna pitika present over the arm) **Past history:** No H/O- any major illness or any known drug reaction.

DISCUSSION

Ayurveda has elaborated the causes and methods of drug-induced consequences along with preventive measures. *Vyapada*, *Viruddha*, *Ahita*, *Atimatra*, *Prakriti viruddha*, Panchakarma *vyapada* etc terms were used in Ayurveda in parlance with present day terms of ADR and Pharmacovigilance of current science. In present case two biscuits two times a day dosage given to a participant. It seems to be a high dose (*Atimatra*) or reactive with the individual (on the basis of *Prakriti*). One biscuit contains 1.25 gm moringa leaves powder so 5 gm was consumed per day. The dose of *Shigru* leaves not found in Ayurveda text but seed and root bark dose has been mentioned. This dose varies from 2 to 8 gram in various text of Ayurveda. Tough it is "*Ksharastikto Vidahakruta Pittarakta prakopanah* |" dose should be less. [6]

Biscuits ingredients i.e. wheat flour, ghee, milk, milk powder and sugar all is of *Madhura Rasa*, *Madhura Veepaka*, *Sheeta Veerya*, *Snigdha* and *Manda* Whereas Moringa has *Kshara, Katu Rasa, Katu Veepaka, Ushna Veerya, Ruksha And Teekshna*.[7-9] Though *Sodium bicarbonate* (*Kshara)* is a salt having *Lavan Rasa* with *Ruksha*, *Ushna* and *Teekshna Guna.* So that an ADR reported in this case might be because of *Guna virodha* (physical & chemical incompatibility). Probably for a thin built girl having 39 kg weight and reduced BMI (16.88 Kg/m^2) with less *Agni* and irregular food habits not able to digest the biscuits, and developed vitiation of *Pitta* along with *Rakta*. This could be the primary reason for development of *Rakta Varna Pitika* with *Kandu* which was observed. *Prakriti* of the patient plays a very important role in the drug administration, and metabolism. So while administering therapeutic dosage, physician should be cautious. Ayurveda practices the individualized medicine based upon the *dosha, dushya,* and *Prakriti*. Combination and permutations of *Prakriti* do propose individual combination and preparations of the products. Thus the additional care should be taken to understand the common ADR developed due to simple dietary products. Bhavamishra has described principles of food products (*Kritanna*) are much more useful in this regard. *Pitta* can be explained in the form of *drava pitta* and *adrava pitta*. When fluid content of *Pitta* is high, it works same as vitiated *Kapha*. This increase of fluidity in the body alters *Kapha* and may lead to report *Kandu*. Simultaneously increasing liquidity (*dravatva*) leads to decrease in *Ushna guna* of *Pitta*. Due to decrease of *Ushna guna,* the *pachana* activity of *Pitta* is hampered and leads to *Agnimandya*. If *Ushna* guna of *Pitta* is increased, causes imbalance of *Pitta* and substantially *drava guna* decreases; which may result in shrinkage of cell. As a result of *Pitta* vitiation, metabolism diminishes and cell damage may occur. Cell damage in due course may cause cell death or cell debris may increase (excessive dryness) to give a reactionary to cause of *Dadru* or *Pitika* over skin. This condition leads to *Kandu*.[10]

The idea behind selecting prescription mentioned in Table-2 was to eliminate the *Pitta* through *virechana* and regulates of the vitiated *Pitta* by internal consumption and external application of medicine. After three days of treatment rash was minimised and itching was totally subsided (Fig a,b,c,d). Then all medicine withdraws and only *Shatadhauta ghruta* was asked for external application.

Before treatment	After 3 days
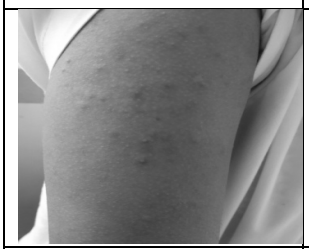	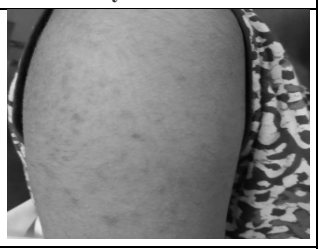
Fig-a Red Rash over arm	Fig-c Minimised the rash over arm
	
Fig-b Red Rash Over back	Fig-d Minimised the rash over back

Probable mode of action of treatment:

Avipattikar Churna is an Ayurvedic herbal medicine used for hyperacidity, gastritis, burning ache due to excess acid, loss of appetite and indigestion linked with gastritis, piles, urinary problems, difficulty in micturition and kidney stones. It is even beneficial for the management of constipation and gastritis. *Avippatikara churna* acts on digestive system through regulation of Liver a seat of *Pitta* and gastric motility and stimulates the production of digestive enzymes that helps in proper absorption of nutrients and inducing intestinal movements. As it induce intestinal peristalsis, in high dose acts as a purgative also. Due to the inducted purgation, *drava* or *adrava pitta* is eliminated from the body as well as other accumulated digestive bio-waste i.e. toxins or *Ama*. *Avipattikara churna* regulates the *sama Pitta* also. *Avipattikara churna* helps in elimination of *Pitta* which is responsible in manifestation of *twak roga* (skin disorders) and *pachana* (digestion) of *Ama* (undigested material).[11]

Laghusutashekhara Ras (LSR) is drug of choice in any rash or reaction. It contains *Swarna gairika, Sunthi* with *Nagavalli swarasa bhavana*. *Swarna gairika* has *Pruthvi mahabhuta* dominance and *Sheeta veerya*. Hence LSR encounters the *Ushna*, *Teekshna*, *Vidahi* and *dravata* of *Pitta* with *Sheeta* and *Parthiva guna* respectively. LSR acts on *Pittaj shirashula, ardhavabhedaka* (migraine), *suryavarata* (sinusitis), *pittaj unmada* (insanity due to pitta dosha), *daha* (burning sensation), *urdhava raktapitta* (bleeding from orifices of the upper part of the body), *mukhapaka* (stomatitis) and especially on acid peptic disorders. *Sunthi* and *Nagavalli* stimulate the digestive enzymes and regulate the *Agni*. If in this condition vitiated *Pitta* is primarily responsible factor, the LSR is safe and effective to rule out the pathology underneath. It balances the pH of the stomach and normalizes the acid base balance in the gut and acts as anti-histaminic.[12]

Shatadhauta ghruta externally acts as healer on itching by *Snigdha guna* and pacify the *Pitta* due to *Sheeta veerya*. In further the *Ghruta* has *ropana* action to limit the allergic rash appeared on the skin. It is mentioned in traditional texts for the management of conditions like burns, chicken pox, scars, wounds, herpes, leprosy, and other skin diseases and as a vehicle for drugs to be applied externally.[13] As it is washed with water (*Shatadhauta*) increase in moisture content may be useful for skin hydration and cooling effect, which can justify its use for the treatment. *p*H change from acidic to neutral makes it beneficial to prevent skin irritation. Reduction in particle size makes the product nongranular, non-sticky, homogeneous, which makes it easy to apply on skin and may result in increased rate of absorption through skin. Due to washing (*Shatadhauta*) results in homogeneous mass of *ghruta* in water emulsion with better consistency and viscosity. Therefore it is helpful for topical application.[14, 15]

CONCLUSION

The present reported ADR is an herbal food product meant for regulation of iron deficiency anaemia; caused the skin rash and itching. This observation cautions us to understand the judicious usage of any herb in the combination as dietary product also. Reporting and analysis of the ADR makes us to realise the Ayurveda principles of *Rasapanchaka* and combination regulations of two or more herbal ingredients. The dose regulations are very important based on *Prakruti* and *Dosha* of the individual. It is only the case observed therefore sufficient adverse drug monitoring is required for *Moringa* enriched biscuits.

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