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Anukta Dravya Adhyayan – Stevia Rebaudiana

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ABSTRACT: -

The emergence of chemical molecules has been a blessing for combating several diseases, but it has paved the way for troublesome situations such as various adverse effects, the emergence of resistance and so on. Various research has been underway on new molecules to find out the least effects and having a better potency is currently on its way and more concentration is being given upon traditional plants in order to avoid these aforementioned problems. Medicinal plants have been recognized to have potential drug uses. Any dysregulation is avoided due to the sweetness imparted by its glycosides and is known by it. The evaluation by phytochemical studies concluded the existence of tannins, alkaloids, glycosides, saponins, sterols, triterpenes with various potentials.^{[5][6]} The purpose of this review is to understand the medicinal potential of stevia and its acceptance as a significant raw material for human diet.

Key Words: Stevia rebaudiana, *Rasa*, *Virya*, *Vipaka*, anti-tumorous activity.



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INTRODUCTION

Ayurveda is an archaic and experimental science of life, explains the principles for the maintenance of health and eradication of disease. The normal drug discovery course of “Laboratories to Clinics” in Ayurveda actually becomes “Clinics to Laboratories”- a reverse Pharmacology Approach. In Ayurvedic Medicine Research, clinical experiences, observations or available data becomes a starting point in conventional drug research, it comes at the end. Thus the drug discovery based on Ayurveda follows a “Reverse Pharmacology” path. Concept of *Anukta* is one such time tested principle which is helpful to understand new disease, drug and formulation.

The word *Anukta* is derived from root vac with negation attached to the basic root. Thus *Anukta* literally means Unsaid or Unuttered. Concept of *Anukta* is stated in the context of *Tantrayukti*. Specific *Tantrayukti* i.e., *Atidesha Tantrayukti* is attributed to understand the concept and technology of *Anukta*. *Anukta Dravya* is basically not included in classics of Ayurveda.

Necessity of Anukta Vichar-

However, several survey states that, more than 5000 medicinal plants are in use by traditional medicine. No details apart from their popular usage in certain disease conditions are known. However they carry a great potential to enhance Ayurvedic Materia Medica. *Anukta* concept is given importance because of the regular additional of new medicinal plant -New Drug.

1. Need of alternatives in case of highly demanded, but endangered medicinal plants.
2. To unravel the hidden treasure from in-situ and ex-situ conversation of medicinal plants.
3. Exploring the folklore knowledge to the society with new emerging diseases.

Methodology involved in introducing Newer Drug

Complete description of medicinal plants (*Anukta*) in terms of Pharmacogenetic and dynamic properties i.e., name, identification, morphology, *Rasapanchaka* etc. may not be available in the Ayurvedic texts. There is a need to first demarcate, identify, nomenclature and analyses them scientifically in terms of *Rasaadi*. Simultaneously, plants should be described botanically and evaluated for phytochemicals so that they can be successfully utilized in therapeutics and documented by incorporating into Nighantu for future references. Thereby adding to Ayurveda Pharmacopeia of India legally after proper researches.

1. Collection of data- through folklore, (RAP) Rapid Assessment Program, comprehensive survey of Literature.
2. Identification- knowledge of local name, consideration of all relevant texts for Taxonomy and Pharmacognosy.
3. Nomenclature – Sanskrit Nomenclature should be done as per the criteria of nomenclature mentioned in Dhanwantari Nighantu.
4. Experimental trial-Toxicological study -to fix dose, dosage form and routine of administration, metabolic tests, investigating pharmacokinetics, efficacy studies.
5. Clinical trial – Phase 1 to Phase 4.

DISCUSSION

Botanical Description of Stevia

A wooden shrub of its kind, Stevia can reach up to 80cm in height when it fully matures. The Stevia genus comprises of at least 110 kinds of species but there might be as many as 300. The habitat of Stevia extends from the Southwestern United states to the Brazilian highlands.^[7] There

are estimated to be over 250 species of *Stevia* that grow wild around the world. However, sweetening properties have been found in *stevia rebaudiana* and in some other species. *Stevia* is a short plant that grows up to 1m tall. The leaves of *stevia* are sessile, elliptic, 3-4 cm long. The stem is woody and weak-pubescent at the bottom, with the root

system of the plant being extensive. *Stevia* has white flowers containing a pale purple throat, they are small in size and arranged in the form of small corymbs.^[1]

Taxonomic information of *stevia rebaudiana* is present in Table 1.

Table 1: Taxonomic information of *Stevia rebaudiana*.

| Taxonomic Information | |
|-----------------------|--------------------------|
| Botanical name | <i>Stevia rebaudiana</i> |
| Kingdom | Plantae |
| Division | Angiosperms |
| Class | Eudicots |
| Order | Asterales |
| Family | Asteraceae |
| Genus | <i>Stevia</i> |
| Species | <i>S. rebaudiana</i> |

Chemical Description of *Stevia*

Diterpene glycosides are responsible for its high sweetening potential of the leaves. Steviol glycosides, are extracted. It is further recognized as Stevioside, Rebaudioside, Steviolbioside And Dulcoside.

The highest amount of glycoside found in *stevia* is stevioside. Stevioside found is 4–13% of dry weight in the *stevia* leaves, rebaudioside is 2–5% and dulcoside 0.4–0.7%. Stevioside accounts for up to 13% of all glycosides in *Stevia*. It is bitter or stringent to taste. Pure stevioside is 300 times sweeter than sucrose was analysed by a Comparative organoleptic at a concentration of 0.4%.^[8] Kroyer^[9] reported the stability of steviosides at various processing and storage conditions. Rebaudioside is 250–450 times sweeter than sucrose and it is found in *stevia*

rebaudiana at 2–5% of dry matter when compared. It is the most stable of glycosides and has no bitter aftertaste, in contrast to the steviosides. Sweet leaf shows presence of diterpenes and triterpenes along with diterpene glycosides.^[10] The metabolization of rebaudioside by intestinal microorganisms produces stevioside which is further transformed into a molecule of steviol and glucose.

Phytochemical Constituents

Microbial infestations or infestations by pests are defended off by the plants with the accumulation of secondary metabolites called phytochemicals. Phytochemicals are active ingredients with therapeutic properties considered as a medicine or drug.^[11] The phytochemical properties of bioactive chemicals present in *stevia* leaves are enlisted in Table 2.

Table 2: Medicinal properties of phytochemicals present in stevia.

| Phytochemicals | Medicinal Properties | References |
|----------------|---|------------|
| Phenols | Anti-apoptotic, anti-inflammatory and anti-aging properties of plant | [21] |
| Saponins | Anti-bacterial agents, surface active and foaming agents, applied in detergents, used to treat diabetes and obesity | [11] |
| Flavonoids | Anti-allergic, anti-cancer, anti-microbial, free radical scavenging activity, prevent oxidative damage and intestinal disorders | [12] |
| Alkaloids | Pain removing medications | [19] |
| Tannins | Used in treating diarrhea and dysentery, wound healing properties | [31] |
| Steroids | Regulate the immune system and reduce the hyper-cholestrolemia | [30] |
| Coumarins | Prevent hyper-proliferative skin diseases | [31] |

Nutritional Composition of Stevia Leaves

Stevia is a low calorie sweetener and the dry leaves, on the basis of its weight, provide an energy of 2.7 kcal/g. Stevia leaves are beneficial due to their nutritional composition because it is a significant source of proteins, carbohydrates and crude fiber that maintains the well being and

decreases the risk of different diseases.

2. The vital source of energy in stevia leaves is by carbohydrates due to the presence of poly and fructo-oligosaccharides, which regulates the metabolism of lipid and reduce the sugar level in blood.^[3] There are traces of mineral elements in dried leaves necessary for metabolic processes in body.

Table 3 gists about the mineral contents of dried stevia leaves .^[15]

| Sr. No. | Nutritional aspect | Quantity | Ref |
|---------|--------------------|----------------|-------|
| 1. | Fat | 1.9-4.34/100gm | 12,13 |
| 2. | Carbohydrate | 52-64.06 | 12,13 |
| 3 | Protein | 10.0-18.0 | 12,13 |

Metabolization of Stevia in Human Body

Stevia leaves contain no calories, stevioside and rebaudiosides which are 300 times sweeter than sucrose possessing more dissolving power in any aqueous solution like water and a

positive taste profile that are metabolized by human body without impacting any health hazards. The pathway for absorption and excretion of steviol glycosides is similar in both humans and animals.^[16] Metabolization

process of rebaudioside in the digestive tract is started by colon microbes which are converted into the stevioside that are further metabolized into steviol and glucose. Glucose which is formed in this process, is directly used by the bacteria present in the colon rather than absorbing in blood stream. The benefit of using Stevia leaves is that post processing there is absence of accumulation of any by product in the human body since all the excess components are expelled out through urine. Furthermore, qualitative and quantitative

resemblances are identified among the gut microflora of physical body and rats.^[17] Another study conducted on to the human gastro-intestinal tract details that the metabolized form of stevia is not modified in low and high concentrations as observed by feces, study also indicated that much of the steviol glycosides are absorbed and remaining are released by urine through kidneys with the assistance of glucuronide bond. Whereas, petite quantities of glucuronide excreted through fecal mass.^[18]

Table 3: Proximate and mineral contents of dried stevia leaves

| Proximate Parameters | Contents g/100g | Minerals | Contents mg/100g |
|----------------------|-----------------|------------|------------------|
| Moisture | 6.7 | Iron | 34.2 |
| Ash | 11.5 | Sodium | 184.3 |
| Fat | 4.2 | Potassium | 2500 |
| Protein | 18 | Calcium | 534.43 |
| Crude fiber | 14.89 | Magnesium | 465.35 |
| Carbohydrates | 30.4 | Phosphorus | 305 |
| | | Chloride | 49.5 |

Caloric Content of Steviosides

It has been shown that there is no absorption of stevioside in human body by the oral route and none of the digestive enzymes of the gastrointestinal tract are incapable to degrade stevioside in its aglycone: steviol. It is crucial to consider that the bacteria present in human colon bring about transformation of stevioside to steviol. The excretion of stevioside from the urine and faeces without being absorbed contributes to its zero calorific value.^[17] Certain tests of digestion and absorption performed with

stevioside compounds shows the effect of gastric juices and digestive enzymes on them and their inability to degrade the compounds. The in vitro digestibility of steviosides by various digestive enzymes examined extensively for many years; proved that none of the enzymes present in the digestive tract digest stevioside, rather hydrolyzation by colon bacteria into both steviol and steviol-16, 17 alpha-epoxide was observed. Later, steviol 16, 17 alpha-epoxide was again converted to steviol, that was expelled from the body in the urine as steviol glucuronide.^[19] This whole process emphasizes on why *stevia*

rebaudiana does not provide calories to the human body.

Effects of Steviosides Consumption on Human Health

About the characteristics of *S. rebaudiana*, several studies have been published that states its antimicrobial, antifungal, hepatoprotective, hypoglycaemic (aqueous extract), antitumor, anti-rotavirus, anti-HIV, antihypertensive, antiviral. One of the most popular usage of stevia and stevioside (mainly in Latin America and the East) include stimulation of alertness and as a supplement against fatigue; it is also attributed a considerable amount of physiological improvement in the process of digestion and other gastrointestinal functions; in addition to regulating blood glucose levels, help in the recovery of liver, pancreas and spleen.^[18] Many of these effects mainly due to the presence of phenolic compounds in the plant (in the leaves and, to a lesser extent in the stem), said compounds are commonly found in both edible and inedible plants. They are vital for the plant for its normal development of growth and defense against the attack of bacteria, parasites, infections, and injuries. The presence of these compounds in injured plants has an important effect on oxidative stability and microbial safety. Phenolic compounds have no known nutritional function, they are important for human health owing to their antioxidant potential.^[20]

Antioxidant activity

Oxidative damage is caused to biological materials on biomolecules such as proteins, nucleic acid, lipids, and carbohydrates. Oxidative stress is a result of a disproportionate secretion of reactive oxygen species (ROS) and the ability of human body to voluntarily detoxify the free radicals in order to repair the subsequent impairment. In vitro, the antioxidant activity of

the Stevia extract was confirmed by diphenyl-1-picrylhydrazyl-hydrate (DPPH) radical scavenging assay, FRAP (ferric ion reducing activity) assay, and phosphomolybdenum assay.^{[30][31]} The methanolic and aqueous extract of the dried Stevia leaves are enriched with polyphenols like hesperidin, ellagic acid, chlorogenic acid, eugenol, coumarin, vanillin and flavonoids and thus are a significant source of antioxidant in food and beverages and very efficient for diseases like diabetes, cancer, neural disorders, arthritis and aging which is caused by the production of ROS. The potentiality of Stevia antioxidants is that it supersede the synthetic antioxidants like BHA (Butylated hydroxyanisole) and BHT (Butylated hydroxytoluene), which recently limited in its use due to their carcinogenic potential.^[32]

Hydrogen peroxide, abiotic stress elicitor results in an increased steviol glycoside production like rebaudioside and stevioside and non-enzymatic antioxidants that has a defensive role against oxidative stress caused by hydrogen peroxide.^[31] The antioxidant activity of phenolic compounds is brought by the radical scavenging by donating hydrogen. Other radical quenching mechanisms includes donation of electron and singlet oxygen quenching.

Antitumor effect

Stevioside shows a marked effect against various cancers like skin cancer, ovarian cancer and breast cancer as studied in various cell line studies. The mechanisms for antitumor effects, as it is brought by the the apoptosis induced reactive oxygen species that scavenge free radicals, increase the expression of apoptotic proteins like Bax, Bcl-2, caspase 9 and reduces the cell viability by inhibition of DNA synthesis and induces cell apoptosis. Iso-steviol, a breakdown

product of stevioside, manifests an inhibitory activity against the enzymes DNA polymerase and DNA topoisomerase II and inactivates P13K/AKT that signals pathway by inhibiting phosphorylation of P13 and AKT. From the methanolic extract of Stevia one compound was isolated and further confirmed by NMR to be centaureidin, that is considered to have antimetabolic effect which can be utilized for tumor therapy.^{[31][34]}

Antibacterial and antifungal activity

Scientists use different solvent extracts (methanol, ethanol, ethyl acetate, acetone, petroleum ether, chloroform) for investigation of the antimicrobial activity of Stevia leaves. Stevia restricts the growth of certain bacteria and other infectious organisms. In some antimicrobial activity screening studies, these extracts exhibit susceptibility to inhibit the growth of certain pathogenic bacteria such as *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhi*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Vibrio cholerae*, *Aeromonas hydrophila*.^[31] Antifungal activity was observed against *Alternaria solani*, *Fusarium oxysporum*, *Aspergillus niger*, and shows maximum zone of inhibition brought by methanolic plant extracts of *stevia rebaudiana* in the study of Arya et al.^[39] Therefore, plant extracts and phytochemicals with known antimicrobial properties are of great significance in therapeutic treatments. The presence of phytochemicals in leaves contributes to the antibacterial activity

Determination of Rasa of Stevia-

Stevia leaves contain a no calorie, stevioside and rebaudiosides which are 300 times sweeter than sucrose. Thus Stevia, itself is an artificial sweetener.

To assess the 'Rasanirdharana' of *Stevia rebaudiana* leaves.

Determination of Rasanirdharana:

This part deals with the assessment of *Rasa*, following *nipata* method of leaf, and *Panchang* of *Stevia rebaudiana*.

Hence the *Rasa* of Stevia is *Madhur rasa*, *Tikta rasa* is its *Anurasa*.

Characteristics of *Madhur rasa-*

("Snehana prinana alhadanam mardavahai roopa labhyate

Mukhastho madhuraschasyam vyapnuvalimpativ cha.")

Cha su .26/74

("Tatra yaha paritoshamutpadyati prahladyati tarpyati jivyati mukhalepam janyati shleshmanam cha abhvardhyati sa madhurah.

Tesham vidyadrasam swadum yo vaktramanuimpati

Aswadyamano dehasya ahladnoaksha prasadnaha

Priyah pippalikadinam.....")

Ash. Hru Su 10/2

"Tatra madhuro rasah sharir satmyadra rasa rudhir mansa medo asthi majja ojaah shukrabhi vardhana

Ayushyah shadindriyaprasadna bal varnakarah pitta visha marutghna trushnadah prashamnastwachyah

Keshyah kanthyo balyah prinano jivanastarpanah bruhana sthairyakarah kshinakshat sandhan karo ghran mukh kanthostha jivha pralhadna daah murcha prashamnah shatpadpipalikanamistitah snigdha shit guruscha."

Cha su 26/43

The Madhura rasa is formed by combination of *Prithvi mahabhuta*. *Madhura rasa* being *satmya* or attuned to the tissues of the body, increase in the *Rasa Dhatu, Rakta, Mamsa, Meda, Asthi, Majja And Shukra Dhatu*. The *shukra dhatu* here not only represents seminal fluid but also internal secretions of the testis which determines and regulate the male sexual characters. According to Ayurveda *ojas* is the final outcome of the *Aharaparinaman*, or the metamorphosis of food into tissue elements. *Madhura rasa* is *vaat shamak, pitta shamak* and *kapha vardhak*.

Here, Stevia brings about the *Dhatuposhan* activity of *Sharira* by bringing about the nourishment of all dhatus. Thus enhancing the nutrition of body.

Determination of *Vipaak* -

Table for derivation of *Katu Vipaak*-

| Sr no | Lakshana | <i>Vipaak Nirdharan</i> |
|-------|--|-------------------------|
| 1 | <i>Srishtavinmutrata</i> (the Amount of waste eliminated from body is more) | <i>Madhura</i> |
| 2 | <i>Srishtavinmutrata</i> (the Amount of waste eliminated from body is more) | <i>Amla</i> |
| 3 | <i>Badhavinmutrata</i> (the amount of waste eliminated from body is less) | <i>Katu</i> |

The above lakshanas were compared in enrolled 30 volunteers for consecutive 7 days. It was observed that 86% of volunteer showed *Badhavinmutrata*.

This is indicative of Stevia being *Katu Vipaaki dravya*.

Benefit of using stevia leaves is that after processing there is no accumulation of any by product in human body because all the excess components release through urine. Furthermore, qualitative and quantitative resemblances have been identified among the gut microflora of human body and rats. Another study which was conducted on to the human gastro-intestinal tract determines that that metabolized form of stevia is not modified in low and high concentrations as observed by feces, study also indicated that much of the steviol glycosides are absorbed and remaining released by urine through kidneys with the help of glucuronide bond. Whereas, minute quantities of glucuronide excreted through fecal mass. The above data shows that Stevia enhances metabolism, also the amount of waste removed from body is less.

The effect of Stevia on mala-

The Above observation also shows that, Stevia reduces the amount of Sweat(*sweda*), urine (*mutra*), and faecal matter (*purisha*) from the body.

The effect of Stevia on Dosha-

| Sr No. | Lakshana | Observation |
|--------|--|---------------------------------------|
| 1 | <i>Madhura Rasa</i> brings about increases in <i>Kapha</i> | It was observed in all the volunteers |
| 2 | <i>Madhur Rasa</i> brings about decrease in <i>Pitta</i> | It was observed in 75% volunteers |
| 3 | <i>Madhur Rasa</i> brings about decrease in <i>Vata</i> | It was observed in 86% volunteers. |

Stevia by its Madhur rasa Majorly aggravates the *Kapha* in the body. It alleviates the *vata* and *pitta*.

The effect of stevia on dhatus-

| Sr no. | Dhatus | Impact of <i>Madhur rasa</i> |
|--------|---------------|---|
| 1 | <i>Rasa</i> | <i>Prinana</i> (nourishes the Dhatu) |
| 2 | <i>Rakta</i> | <i>Poshan</i> (nourishes the Dhatu) |
| 3 | <i>Mamsa</i> | <i>Bruhan</i> (increase in volume) |
| 4 | <i>Meda</i> | <i>Bruhan</i> (increase in volume) |
| 5 | <i>Asthi</i> | <i>Sthairyakar</i> (Brings stability) |
| 6 | <i>Majja</i> | <i>Poshan</i> (nourishes the Dhatu) |
| 7 | <i>Shukra</i> | <i>Shukravardhan</i> (increase in volume) |

To observe the Changes in dhatu the enrolled volunteers were administered with the Drug for a period of dhatus following the *Dhatuposhan nyay*. It was observed that there was weight gain in the volunteers, and a major change was observed in *Mamsa* and *Meda* dhatu which was examined by the *Mamsa* and *Meda dhatu Karma*. Stevia because of its calorific value is highly nutritious for the *Dhatus*. It is nutritive for all the seven *dhatus*.

Priorly the action of stevia is more in ***mamsa and meda dhatu***.

The above karma of Stevia makes it an apt drug of choice in Cancer Patients.

Focusing on its *karma*,

The above reference of researches is indicative that, Stevia has *Dipaniya* and *Pachaniya* action.

It also has *Bruhan* action on the body.

Dravya derivation-

| Sr no. | Rasa | Virya | Vipaak | Dravya |
|--------|---------|-------|--------|---------------------------|
| 1 | Madhur | Shita | Madhur | Samanpratyayarbdha dravya |
| 2 | Amla | Ushna | Amla | Samanpratyayarbdha dravya |
| 3 | Lavana | Ushna | Madhur | Samanpratyayarbdha dravya |
| 4 | Katu | Ushna | Katu | Samanpratyayarbdha dravya |
| 5 | Tikta | Shita | Katu | Samanpratyayarbdha dravya |
| 6 | Kashaya | Shita | Katu | Samanpratyayarbdha dravya |

CONCLUSION

The Above table details about the *Samanpratyayarabdha dravya*. The following study shows Stevia as *Madhura Rasatmak Dravya and Katu vipaaki*. Thus here it goes against the law of *Samanpratyayarabdha dravya*. Thus Stevia is a *Vichitrapratyayarabdha Dravya*.

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