J. Indian Dietetic Association Volume 40, No.1, pp. 40-44, 2017

Natural Anticancer Activity of Stevia - A Review

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INTRODUCTION :

New study of 2017 crowns STEVIA as The King of Sweetener. [1] Stevia is an exceptional plant based sugar substitute that has effective anti carcinogenic properties.It belongs to the *Asteraceae*family so it's related to ragweed, chrysanthemums etc. *Stevia rebaudiana*Bertoni is themost prized originated variety among all. *Stevia rebaudiana*genius was discovered by Petrus Jacobus, Professor of Botany at University of Valencia. [2] It is originated from tropical and subtropical area of America, known as sweet herb. The sweetness of stevia leaves is caused by eight glycosides viz. Stevioside, Rebaudioside A, C, D, E, F, Steviolbioside and Dulcoside A. The active compound of stevia are steviol glycoside, mainly stevioside and rebaudioside which have up to 150-300 times sweeter than sugar, these two glycosides were isolated by Chemist M. Brider and R. Lavielle. These are heat stable, pH (6.5-7.5) stable, and not fermentable. [2] Stevia lowers blood pressure, and acts as a high sugar antagonist, as well, interact with anti-fungal, anti-inflammatories, anti-microbial, anti-viral, appetite suppressants, calcium-channel blockers, and cholesterol lowering drugs, drugs that increase urination, fertility agents and other medications. Stevia improves glucose metabolism and break down of fat and bile acids which reduce the cause of Diabetes and Obesity. In India since 13 Nov 2015, Food Safety and Standards Authority of India or FSSAI has permitted itsuse which includes carbonated water, dairy based desserts, flavored drinks, yoghurts, ready-to-eat cereals, fruit nectars and jams, madhu-tulsi.etc.

The anticancer activity of extract of stevia leaves is determined since last few years, though earlier, many accused stevia for being the reason of carcinoma. Moreover, scientists have proven that the active molecules of stevia help to prevent cancerous cells. Additionally, it has effective healing properties and maintains 'Zero' Glycemic Index. Stevia degrades the causes of Diabetes Mellitus and Obesity which are the important etiology of Cancer. [3] So, the objective of this study is based on how much advantageous is this traditional oriental

medicinal herb in order to perform ethno medicinal activity such as ANTICARCINOGENIC ACTIVITY. [4]

REVIEW OF LITERATURE :

Eminent Researchers, world wide, are experimenting vastly in-vitro and in-vivo tests to elucidate this matter.

IN-VITRO STUDY :

Same aged 150-250 kg of Swiss Albino mice of either sexwas selected and each group consists of 6 mice. They were fed with standard diet and water ad libitum. By continuous extraction using Soxhlet apparatus, the ethanolic extract of *Stevia rebaudiana* (EESR) was obtained which is the key material of the study. Then Ehrlich Ascites Carcinoma (EAC) cells ascetic forms were inoculated (10^5 cells/mouse). After transplantation of tumor cells, many neoplastic cells were produced. Group 1 received normal saline 1mg/kg/p.o with carcinoma induced mice. Group 2 & Group 3 received ethanolic extract of Stevia *rebaudiana* 100 & 300 mg/kg/i.p respectively. Group 4 received 5 fluoro uracil in 20 mg/kg/i.p. Thereafter the observation was done for furtherelaboration. [5]

It is already shown that many researchers have gone through diverse experiences and display intensive practical proofs regarding this topic. It was discovered that, 12-O-tetradecanoylphorbol-13-acetate or TPA intensively existed in mice which is a potent carcinogen and it was shown that practically the steviol molecules successfully blocked it. By inhibiting the effect of TPA, it might have a negative role of spurring cancer growth. It can be stated that the tumor inhibiting activity of EESR against EAC strain is logical.

But still, there will be more investigations the mediation of stevia. Cytological changes like reduction in mitotic activity, appearance of membrane blabbing and intra cytoplasmic vacuoles in tumor cells indicate that EESR may have direct tumorocidal affection on tumor cells. There is an increased life span, Hemoglobin level, Red Blood Cell count, glucose, protein, urea, uric acid level, decreased tumors volume, total cell count, body weight, packed cells volume, Cholesterol in dose dependent manner and most importantly stevia has dose dependent characteristics in compare with other drugs. Now-a-days, cancer patients are treated with natural methods with herbs and high dose nutrient injects. [5]

In an another study done on 344 rats given diet with 5% stevia the high intake did not show any sign of cancer after had been observed. [12]

On this in-vitro study it was highlighted after the minute observation, no carcinogenic symptoms appeared in those rats in fact after 108 weeks of ingestion of stevia.[12] Thus, it can be noted that, stevia could not contribute any adverse mechanism which had been in doubt once by Nutrition Advocate Centre for Science in the public interest.

IN-VIVO STUDY :

On the other hand, 36 derivatives of steviosides from stevia were placed on leukemia, lungs, and stomach and breast cancer cell lines. [6]

On case of the in-vivo study, that cytotoxicity is treating cell fates and turns into necrosis which results cell lysis along with

degraded integrity of membrane. Then it is stopped growing and cell viability gets hampered. This is a genetic program to combat against cancer. [6]

In this respect, another elaborated study can be enlightened here. In this experiment *Stevia rebaudiana* ethanolic extract (SREE) was examined for antioxidant property specifically free radicals scavenging and anti proliferating effect in cervix, pancreatic and colonic cancer cells. These mechanisms are confirmed by testing the effects on Cyclin D1 CDK4. Some bio assays were also performed diterpene glycoside stevioside. [7]

Many claims after brief evidence, stevia is 'safe and non-toxic' and has no after taste. But the fact is it is not the key material to cure cancer but use as dietary supplements to prevent it. [9] And, in the last study related to anti oxidant properties which stretch the way for preventing this degenerative disease, found that SREE helps to scavenge the free radicals in the body and proliferates cell death in three cell lines. It inhibits CDK4 and maintains anti proliferated properties in the cell. [7] It is known that excessive free radicals damage the cells that cause mutation leading to cancer. Some antioxidants present in stevia are kaempferol, quercetin, chlorogenic acid, caffeic acid, isoquercitrin and isosteviol.

According to the 2002 “Chemical and Pharmaceutical Bulletin,” it was explained that most of the compounds extracted from stevia leaves do not exhibit mutagenic or genotoxic effects that can cause effects cancer.However, they did observe that stevioside was converted to a molecule by bacteria which have mutagenic effects. But rebaudioside A which is the main component of stevia, has no as such genotoxic effects is therefore, proved that stevia has no carcinogenic property.[11] In short, stevia is non Genetically Modifiedand the sweetest part of the stevia leaf is rebaudioside A which is extracted under organic harvesting. But simultaneously, Stevioside compound is exhibited with mutagenic condition by mixing stevioside with silicates, starches, and other low cost bulking ingredients for business purpose, act reciprocally. Furthermore, most raw and less processed stevia products contain both sweeteners, whereas most highly processed forms of stevia, like Truvia, only contain the rebaudioside, theFood and Drug Administration (FDA) recognized stevia as safe and suitable.Whatever, rebaudioside better tastes, sweet and least bitter in compare to stevioside.

Another important matter to be discussed in recent times, that is, inseparable relation between sugar intake and cancer. As we all know, having diabetes or signs of insulin resistance may lead to an increased risk of certain cancers. If sugar consumption gets elevated the survival rates in any stage of cancer creates a barrier and tumors grow when blood sugar rises. Whatever the sweetness factors exist in stevia but the sweet molecules of it does not attack the blood stream like other sweeteners. Cancer thrives when it gets glucose delivered to it by the blood. In short, a statement can be established that the sweetener, stevia can give the sweet tooth to treat while depriving the tumor of sugar. [8]

According to Acceptable Daily Intake (ADI), 4 mg/kg of body weight/day of stevia would not be genotoxic.There are different types of stevia extracts available in market specially health stores and online, in liquid or powdered form.Rebaudioside is used in powder and liquid forms to heighten sweetened intensity and improve taste. Stevioside or steviol glycoside is a white or off white powder which does not appear in liquid form.Some people prefer the powder over liquid.It has been proven for decade with the minimum usage of naturally derived stevia, harvesting in organic way and contains good flavors but no unnatural additives, are actually not associated with cancer whereas help in preventing to proceed sarcoma.

This graph represents the statistical value of previous and upcoming usage of Stevia, worldwide. So, it is noticed that, people are interested to use stevia more and in future the growth hikes gradually.



Figure – 1 (estimated in 1000 Tonnes)

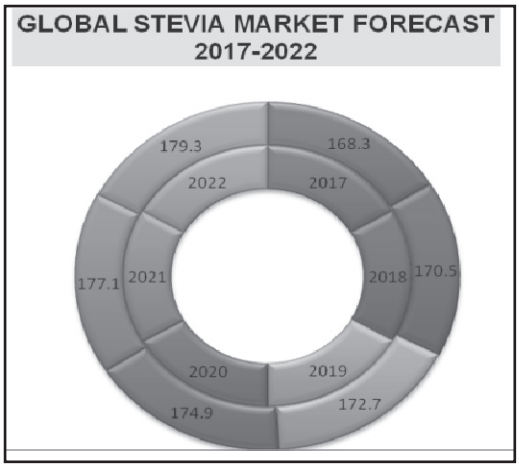


Figure – 2 (estimated in Tons)
SOURCE: IMARC GROUP, 2016

CONCLUSION :

In the mid 70S when popularity of other sweetener brands got down the uses of stevia has been uplifted magically. After years, stevia is used in multinational companies as sweetening agents. But some scientists have argued that the strain of stevia can mutate DNA and may cause a risk of cancer. But this statement is baseless. Many experiments have clinically proved that stevia hinders aggregation of toxicity in the cells. At first, U.S Government did not permit “Crude Stevia Extract” available in the open market. Then Food and Drug Administration (FDA) gave green signal as titled as “Generally Recognized as Safe (GRAS)”, by the notice (GRN-607) in 2016. But the path was not smooth at all. In 1991, FDA marked stevia “Unsafe” as it had toxicological information. Then Dietary Supplement Health and Education Act, 1994 protested against this and the statement was revised. After some years the

steviol glycosides met purity criteria established by the JECFA (WHO) and stamped stevia as a secured sweetener. Beyond the controversies, it is stated the safety of stevia depends upon how it is sold and how it is consumed. Besides, it has versatile functions in case of protecting many complicated diseases and last but not the least, stevia is not only protect the body from the effects of carcinogens linked to numerous health concerns and disorders, but these components actually been shown to limit tumor promoting cell growth. [10]

Based on the published research, independent scientific experts globally have concluded that stevia are safefor people of all ages.

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