Stevia Rebaudiana as an Immunity Booster for COVID-19
Aayeena Altaf1, Mohammad Umar Khan1, Bhavna Jha1, Raj Das1, Manzoor Ganai2*

1Department of Food Technology, School of Interdisciplinary Science and Technology, Jamia Hamdard, New Delhi-110062, India
2Department of Agronomy, Sher-e-Kashmir University of Agriculture, Sciences and Technology of Kashmir, Jammu and Kashmir, India

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*Corresponding author: Manzoor Ganai

Abstract
Stevia rebaudiana is a nutrient rich natural sweetest plant of Asteraceae family. The leaves naturally contain diterpene glycosides (Stevioside and Rebaudioside-A), steviolbioside and dulcoside, which are responsible for its sweet taste. Along with these compounds it also contains functional compounds like phenolic acids, free radical scavenging and antioxidant capability, flavonoids, condensed tannins, anthocyanins, nutraceutical properties, etc. Stevia exhibits strong antioxidant potential as a sugar substitute owing to the presence of various compounds with medicinal significance. However, in large amounts they also possess several beneficial effects on disease in which radicals are involved. As there is no targeted Covid-19 therapy available, Stevia crude extracts and steviol glycosides are suggested to treat Covid-19 patients. Stevia has many pharmacological and therapeutic applications as suggested by many preclinical and some clinical studies, these are nontoxic and possess antioxidant, antimicrobial, antifungal and anticarcinogenic activity. Antioxidants through their scavenging power are useful for the management of various diseases that aids in combating different chronic diseases as well as increase immunity against the severity of various infections like in case of Covid-19. It is also generally accepted that consumption of 5gm dried Stevia leaves is without health problems.

Key words: Covid-19, Stevia rebaudiana, Steviosides, Anti-oxidants and Immunity.

INTRODUCTION
The world population is hit severely by a recent outbreak of new corona virus since December 2019 which is known as severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) causing acute respiratory disease with huge number of deaths till now. The world health organisation (WHO) alerted the infection epidemic on March 11, 2020. Since then, laboratories around the globe have been observed in the growing race of production of efficient vaccine and therapeutic treatment which will help the mankind to return to their normal lives. There is no treatment found till date which is 100 percent efficient in combating the different strains of corona virus. People are taking various preventive measures against the corona virus. There are different factors that determine the severity of the disease like obesity, hyper tension, cardiovascular disease, diabetes as well as lung disease. The people free from these problems have low chance of infection as they have immunity to fight against the severity of the disease. These diseases are related to the imbalance between radicals and antioxidants (enzymatic and non-enzymatic, e.g., Vit C, GSH). It was found that the severity of the disease in China was associated with the deficiency of selenium (se). Its deficiency has been related to the higher susceptibility to RNA viral infections and other serious disease outcome. Seleno proteins are important antioxidant defence systems maintaining redox homeostasis, which also includes Catalase (CAT), Superoxide Dismutase (SOD), Glutathione (GSH), Vitamin E and C, and carotenoids. It was shown that an optimal nutritional status is required for a well-functioning immune system to protect against viral infections. Vitamins such as Vit A, B6, B12, C, D, E and folate and minerals like zinc, iron, selenium, magnesium and copper and omega-3 fatty acids play vital and complementary roles in the support of the immune system (Geuns Jan M.C, 2020). A high dose of Vitamin C that function as a key antioxidant is highly recommended for the treatment of Covid-19. The serum level of vitamin C has been correlated with its cellular immune function, anti-oxidative capacity and neutrophil function (Zarezade et al, 2021). Vitamin D, a steroid hormone is also found to be very effective to deal with the severity of this virus.

Moreover, bioactive compounds like Myricitrin, myricetin, resveratrol, and δ-viniferin, have been found to be potential anti-Covid-19 therapeutics.
Given these molecules target different viral proteins at different stages of viral replication, and a majority of them are common ingredients of the food chain (e.g. Curcumin from turmeric, carnosol from rosemary, quercetin in apples, etc), it can be assumed that consumption of such foods may positively impact protection against SARS-CoV-2 infection (Savant et al. 2021).

Nutraceuticals has always shown its great effectiveness in treating various diseases as well as for the purpose of boosting immunity against different diseases. Stevia might be one of the dominant sources for boosting immunity against covid-19 as it constitutes a good amount of vitamins, protein, lipid, amino acids and minerals. The compounds like alkaloids, glycosides, saponins, sterols, and triterpenes, anthraquinoine, and other reducing compounds are also present along with higher concentration of tannins. Stevia glycosides possess many pharmaceutical properties viz; anti-hyperglycaemic, antihypertensive, antioxidant, antimicrobial activity, anticancer effect, anti-inflammatory and immune-modulatory effect etc (Singh et al, 2019).

Botanical description of Stevia Rebaudiana

Stevia is a branched shrub, which belongs to Asteraceae family, native to the Amambay region in the north east of Paraguay. It is also found in the neighbouring parts of Brazil and Argentina. Presently its cultivation has spread to other regions of the world, including Canada and some parts of Asia and Europe. It grows up 1m tall. (Alahmad, 2018). (Ahsan et al, 2020) estimated that more than 250 species of stevia is found wild around the world. Stevia is a short-day plant that grows up to 1m tall. It has 3-4 cm long elliptic and sessile leaves. The root system of the plant is extensive, the stem is woody and weak-pubescent at the bottom. It has small white flowers with a pale purple throat arranged in the form of small corymbs.

Taxonomy of Stevia rebaudiana.

<table>
<thead>
<tr>
<th>Botanical name</th>
<th>Stevia rebaudiana</th>
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<tbody>
<tr>
<td>Kingdom</td>
<td>Plantae</td>
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<tr>
<td>Division</td>
<td>Angiosperms</td>
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<td>Eudicots</td>
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<tr>
<td>Family</td>
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<tr>
<td>Genus</td>
<td>Stevia</td>
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<tr>
<td>Species</td>
<td>S. rebaudiana</td>
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Chemical components of stevia rebaudiana

Stevia is chemically composed of protein, fat, carbohydrate, ash and fibre. The researchers used different techniques for the composition of stevia leaves extract such as GC-MS, HPLC, and LCMS etc. The sweet leaves of stevia (Stevia rebaudiana Bertoni) have been investigated by many researchers, is used for many years by South America and they call it “Kaa-hee” (Sweet herb) (Khalid et al, 2021). Initially, 9 essential amino acids, i.e., glutamic acid, aspartic acid, lysine, serine, alanine, proline, tyrosine, isoleucine and methionine, were isolated from stevia leaves. Later on, 17 amino acids were isolated. Stevia leaves also contain medically and commercially important several natural nutrients and vitamins such as chromium, magnesium, manganese, potassium, selenium, zinc, and vitamin B3 (Niacin). Phytochemical screening has showed that tannins are present in higher concentrations followed by alkaloids, glycosides, saponins, sterols, and triterpenes, anthraquinone, and other reducing compounds. The chemical composition of stevia leaves changes depending on the degree of their processing (Singh et al, 2019). Along with these compounds it also contains functional compounds like phenolic acids, free radical scavenging and antioxidant capability, nutraceutical properties, etc (Jahangir et al, 2020). The extract from dried stevia leaves contains 10% amino acids, 18% proteins, 33% carbohydrates and 39% reducing sugars, while in the extract from fresh leaves the levels are 25%, 19%, 31% and 25%, respectively. Fat content in dry matter of stevia leaves amounts to 1.9–4.34 g·100 g⁻¹ dm. The chemical composition of this plant is also affected by the method of leaf drying (Marcinek et al, 2015).

IMMUNOLOGICAL COMPONENTS IN STEVIA

Minerals/metals elements are the diet components inevitable for the upkeep of life and good health. Metabolic processes need them for proper functioning; some are required in major quantity while other in minor or trace amount for proper metabolic processes. Stevia is found to be a good source of minerals. Major elements that are present include magnesium, potassium, chlorine, sodium, phosphorous, Sulphur, calcium are classified as macronutrients. However micronutrients include iron, cobalt, zinc, copper, selenium, iodine, molybdenum, manganese, etc (Jahangir et al, 2019). Selenium present in the stevia leaves is good source used against the severity of Covid-19. (Kieliszek et al, 2020) suggested decades ago that selenium may possess cancer-protecting effects in man, and that the selenium-deficient diet in the developed countries may contribute to increased incidence of malignant tumours as well as to increased viral infections.

Stevia contains many vitamins included vitamins A, C and vitamins of B-complex like thiamine and riboflavin. A previous study was shown that stevia contains water-soluble vitamins such as vitamin C and vitamin B complex. In leaves, folic acid was a major compound and after that vitamin C is found in a major concentration. Vitamin A plays a vital role in metabolism and immune response and protects against the severity of the infection. According to (Samad et al,
2021), the three primary active forms of vitamin A include retinol, retinoic acid, and retinal. Hence, they are regarded as anti-infective as many of the body’s defense mechanisms against infections depend on their constant supply. Vitamin E administration among elderly patients is likely to help the immune function, which increases the chances of infection resistance and decreases mortality that could be triggered by infection. Multiple studies regarding vitamin E’s potential benefits to Covid-19 patients indicated that vitamin E and C in combination could be a beneficial antioxidant therapy for cardiac implications of Covid-19. Likewise, vitamin D and folic acid present in stevia leaves also acts as a defensive source against Covid-19.

Anti-oxidants and phenolic compounds
Oxidation is an important biological process essential for the production of energy in the human organism. During metabolism molecular oxygen is reduced to water. In the course of electron transfer free reactive oxygen species (ROS), such as hydrogen peroxide, hydroxyl and peroxide radicals. Free radicals are considered to be the causative agents in the development of neurological diseases, ageing, ischaemic heart disease, stroke, Alzheimer’s and Parkinson’s disease, cancer as well as inflammation and reduced immunity. Leaves of Stevia rebaudiana Bertoni were found to contain polyphenolic compounds exhibiting antioxidant properties. (Marcinek et al, 2015). Stevia exhibits strong antioxidant potential as a sugar substitute owing to the presence of various compounds with medicinal significance such as phenolic compounds, flavonoids, diterpene glycosides (stevioside and rebaudioside-A), condensed tannins, anthocyanins, and phenolic acids (Jiang et al, 2020).

The major symptoms observed in Covid-19 that is reduced immunity and inflammation can be treated with the use of anti-oxidant present in stevia rebaudiana. (Kobus et al, 2015) found that the Polyphenols play an important role in the prevention of many diet-dependent diseases. It has been recognized that flavonoids show antioxidant activity and their effects on human nutrition and health are considerable. Flavonoids and phenolic compounds have been recently correlated with antioxidant properties of Stevia rebaudiana. The mechanisms of action of flavonoids are through scavenging or chelating process. The compounds such as flavonoids, which contain hydroxyls, are responsible for the radical scavenging effect in the plants. Phenolic compounds are a class of antioxidant agents which act as free radical terminators (Mutmainah et al, 2019). Antioxidants through their scavenging power are useful for the management of various diseases. Thus, it aids in combating different chronic diseases as well as increase immunity against the severity of various infections.

Steviol compounds
Several medical problems like diabetes, obesity, high blood pressure coronary heart disease arises due to more intake of sucrose content as it is associated with negative impact on human health. Diterpene glycosides, Ent-kaurene derivatives found in sweet leaf, are responsible for its high sweetening potential. Hence there is an urgent need to substitute sugar with natural low-calorie sweetener like stevia rebaudiana leaves powder which will increase nutritional profile of the product. (Singh et al, 2019). In Europe and the United States, stevia has been approved as a natural sweetener and a food additive with an acceptable daily intake of 4 mg/kg body weight declared by the European Food Safety Authority and the US Food and Drug Administration (FDA), and it was granted generally recognized as safe status in 2008 by the FDA (Jiang et al, 2020). As diabetes is known to be the risk factor of Covid-19 severity, steviol glycosides as known as diterpene compound acts as a vital source in preventing related health issues.

PHYTOCHEMICALS
The results on preliminary phytochemical screening of dry leaves extract of Stevia revealed the presence of alkaloids, tannins, flavonoids, cardiac glycosides, steroids, saponins. Presence of alkaloids was confirmed through Hager’s, Wagner’s and Dragendorff’s test. The presence of phenol, flavonoids and tannins was comparatively high except for aqueous extract which was negative for phenols. Steroids and cardiac glycosides were found to be higher amount in all the extracts. The highest amount of saponin was observed in aqueous and methanolic extract where traces of saponin were found in the ethanolic extract. The alcoholic and aqueous extracts of S. rebaudiana contained steroids, glycosides, tannins, alkaloids and saponins like phytochemicals. (Howlander et al, 2016). These phytochemicals present in stevia have multiple health benefits like resistance to infections, boosts immunity, reduced risk of cardiovascular diseases and so on.

CONCLUSION
This review showed that the Stevia rebaudiana consists many functional compounds which has been proved as an utmost source for various health benefits. The components found in stevia such as anti-oxidant and polyphenols, phytochemicals, vitamins, minerals and steviol compounds influence the above cited diseases, as these are related with the immune boosting source. At the present situation of Covid-19 prevalence around the globe, immunity boosting has become a major concern. As there is no therapeutic treatment discovered which is fully efficient in combating the severity of virus infection, a good immunity is key factor which reduces the chances to get infected. Researchers have found that stevia has many medicinal
properties against the health issues. Due to potent activities of compounds found in stevia, it has been proved as an efficient source to improve the general health due to its special properties and this specifically in the risk groups for Covid-19, mainly patients with obesity, diabetes, hypertension, lung disease and cardiovascular diseases.

REFERENCES