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EMERGING ROLE OF NUTRACEUTICALS IN THE MANAGEMENT OF HYPERTENSION: A SYSTEMATIC REVIEW

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ABSTRACT: Nutraceutical is a word obtained from Nutrition and Pharmaceuticals. Nutrients are a feed constituent that helps to support the life of human beings or animals. Pharmaceutical components are non-toxic food constituents, including prevention and treatment of disease. They commonly inhabit the disorders associated with oxidative stress, for instance, cardiovascular disease, Diabetes, and Hypertension. Nutraceuticals possess substantial importance because of their expected safety and possible nutritional and therapeutic effects. Hypertension is the most frequent risk factor for cardiovascular disease involving coronary heart disease and stroke. There is a crucial role in utilizing single and integral nutraceutical supplements, vitamins, antioxidants, and minerals in the treatment of hypertension. These food supplements rein huge demand because they are less toxic and have long life treatment with dietary food. We have done a face-to-face survey on 33 medical stores. The survey results found that the most demanding nutraceutical is Mactotal, and the least demanding nutraceuticals are Beryl tone and Allvell-Z grape seed extract. The survey study also shows a list of Nutraceuticals that are available in drug stores, including Mactotal, Omega fatty acids grape seed extract, Advanced BP support, Natural formula BP complex, Blood pressure formula, BP rescue, Cholbiome, Zeovita- 4G, Super B complex, Alpha-linolenic acid, Allvell-Z grape seed extract tablet, Antioxidant support, Vegifruit syrup, Beet juice and Beryl tone.

INTRODUCTION: Hypertension is not a disease it is a condition in which the force of blood against the artery walls is high. According to the 2017 American college of cardiology/ American heart association hypertension recommendations, hypertension is defined as systolic blood pressure above 130mmHg or diastolic blood pressure above 80mm Hg¹.

Usually, hypertension occurs when the blood pressure is above 140/90mm Hg, considering if the pressure is above 180/120mm Hg. The Hong Kong cardiovascular prevalence population investigated of healthy people randomly selected; the popularity of hypertension was below 2% in young subjects aged 25-34, but the prevalence rises to around 50% in those 65-75 years of age².

Research has recommended that the blood vessels naturally harden with age, losing their compliance. This may clarify why older people are more likely to modify high blood pressure³. Hypertension disorders in pregnancy are among the most common medical complications, affecting 5% to 10% of pregnancies worldwide⁴. The hypertension

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is divided into two types. Essential or primary hypertension when the condition has no known cause. When another condition causes hypertension, it is known as secondary hypertension⁵. The factors of hypertension are shown in **Table 1**.

TABLE 1: FACTORS OF HYPERTENSION

Essential hypertension	Smoking
Difficulty in breathing	Do not do exercise
Arteriosclerosis	Are over 65 ages
Cushing syndrome	Intake to much salt

Medication of Hypertension: There are some medications which are used in the condition of hypertension:

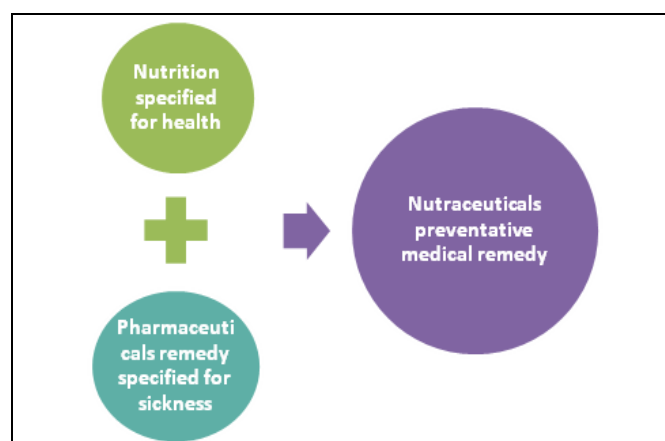
- **Antihypertensive Drug:** Antihypertensive drugs may decrease cardiac output by either inhibiting myocardial contractility or reducing ventricular filling pressure⁶.
- **Non-Pharmacological Management of hypertension:** It is a harmless treatment and helpful either to eliminate the drug requirement or reduce the dose. Non-pharmacological approaches to reducing blood pressure generally treat patients with diastolic blood pressure in the range of 90 to 95mmHg⁷.
- **Reduction of Body Weight:** Obesity and hypertension are closely associated, and obese hypertensive may lower their blood pressure by losing weight regardless of a change in salt consumption⁸.
- **Sodium Restriction:** Severe salt restriction will lower the blood pressure in most hospitalized hypertensive patients; this treatment method was advocated before developing effective antihypertensive drugs⁹.
- **Physical Exercise:** Lack of physical activity is associated with a higher incidence of hypertension¹⁰.
- **Diet:** Natural vegetables and dietary products contain high potassium levels, which lower the BP by increasing sodium excretion, decreasing sympathetic activity, and renin-angiotensin secretion¹¹.

Nutraceuticals: A nutraceuticals word combines 'Nutrient' and 'Pharmaceutical'. According to AAFCO, 1996, 'nutrient' means a feed component

in the form and at an extent that will assist or support of the life of a human being or animal occupy 'nutraceutical' means any non-toxic food constituent that has scientifically demonstrated health welfare, including the treatment of disease¹². Nutraceuticals are defined as-, according to Dr. Stephen De Felice- a "food, or parts of a food, that contribute medical or health welfare including the prevention and treatment of disease¹³. It is also known as "Functional food". The nutraceuticals components elaborated on the other components like dietary supplements, herbal components, vitamins, and nutrients¹⁴.

Hippocrates stressed in the certified means, "Let food be the medicine and medicine be food", concerning 2000years previously^{15, 16}. Nutraceutical components are the product in which the combination of nutrients and functional food are also used as medicine. Nutraceutical products are physiologically useful for the protection against in case of chronic disease, diabetes, cancer, high blood pressure, and Alzheimer's disease¹⁷. The concept of nutraceuticals was started from the survey in U.K., Germany, and France, and its consumer then exercises hereditary factors to achieve an adequate health¹⁸. Nutraceuticals are food derivatives that give therapeutic and health welfare, as well as the obstruction, Management, and treatment of disease, and involve a class the nutrient, encapsulated dietary additives, and frozen food.

Benefits of Nutraceuticals^{19,20}:

**FIG. 1: BENEFITS OF NUTRACEUTICALS**

Nutraceuticals are physiologically health beneficial in many diseases like cancer, heart disease and the treatment of hypertension, diabetes, arthritis, and

nutraceuticals may offer many benefits in human health^{13, 14}. Some benefits of nutraceuticals in human life are shown in **Fig. 1**.

- It increases the value of the diet.
- It may help us live longer.
- It helps us to avoid any particular long-term medical condition.
- It may be more natural than traditional medicine and helps produce less side effect in the body.
- It fulfills the deficiency of nutrients in our body.
- These are easily available in market and market and they are economically affordable.

Types of Nutraceuticals^{21, 22}: The nutraceuticals are mainly divided in two types:

1. Traditional Nutraceuticals: This is the class which we get directly from nature without changing any natural form. Many constituents such as lycopene in tomatoes, saponins in soy are present and ingested for health benefits. Traditional nutraceuticals can be classified on the basis of:

(a) Chemical constituents: Based on chemical constituents the, nutraceuticals can divide into three types:

- **Nutrients:** Plant and animal products with a vitamin have many health welfares and are pleasant in curing heart, kidney, lung disease, etc. The nutrients elaborated the minerals, vitamins, and amino acids, with granted nutritional functions.
- **Herbals:** Nutraceuticals and herbs have a worthy influence on preventing many chronic diseases and producing healthier lives. Peppermint (*Mentha piperita*) carries several terpenoids, mainly menthol, a bioactive component and cures a cold and aches. Tannins contents of lavender assist issuing stress and blood pressure and are convenient for lung disorders.
- **Phytochemicals:** Phytochemicals are the nutrients based on plants with specific biological occupations that encourage human

health. They are further mentioned as phytonutrients. Ex- Flavonoids, Phenolic acids, curcumin.

(b) Nutraceutical Enzyme: Some enzymes are obtained from plants, animals, and microbial origin. Enzymes are a crucial part of life, without which our body is authorized to come to an end of the function.

(c) Probiotic Microorganism: Probiotics manners 'for life'. They are described as live microorganisms, which, when ingested in tolerable aggregates, consult a health effect on the host. Ex- Insulin.

2. Non-traditional Nutraceuticals are food enhanced with additives or biotechnologically designed crops to improve the nutrients. Such as Rice and Broccoli are well off beta-carotene and vitamins. Non-traditional nutraceuticals are classified as follows:

- **Fortified Nutraceuticals are enhanced with vitamins and minerals,** generally at a range up to 100% of the dietary supplements gaining for the nutrient. These are nutraceuticals from agricultural procreation or added nutrients and constituents.
- **Recombinant Nutraceuticals:** Biotechnology implements have been well applied between an agitation process in several food substances such as cheese and bread to extract the enzyme convenient for providing essential nutrients at best level.

Nutraceuticals in Management of Cardiovascular disease Hypertension]: Cardiovascular diseases (CVD) are chronic diseases using disorders of the heart and blood vessels which generally include hypertension [high blood pressure], coronary heart disease [heart attack], stroke, etc.²³.

The nutraceuticals reduce the possibility of cardiovascular by regulating several possible factors such as oxidative strain, and renin-angiotensin structure hyperactivity. Nutraceutical derivatives, antioxidants, vitamins, and natural components in food produce effects that are a class of medications that reduce blood pressure²⁴.

High blood pressure is one of the most relevant independent risk factors of CVDs and the most prevalent all over the world.

Reduction in nitric oxide bioavailability, increase in angiotensin-II and endothelin coupled with endothelial activation initiate the vascular and cardiac dysfunction and hypertension²⁵.

Dietary folate and plasma ascorbic acid has been found to be inversely associated with blood pressure. Lower risk of elevated blood pressure in the multiple supplement groups suggests that there was a relationship between these nutrients and blood pressure²⁶.

Nutraceuticals or the supplements of the nutrients of the nutraceuticals reduces the hypertensive condition by lowering blood pressure and increasing antioxidant enzymes.

“Antihypertensive” Foods, Nutrients and Nutraceuticals: The European society of hypertension [ESH] specialists board has published a paper on nutraceuticals and BP control that assorted the natural compounds with clinically measurable consequences on BP in foods, nutrients, and non- nutrient nutraceuticals²⁷.

“Antihypertensive” Food: It is a food supplement that is used to reduce high blood pressure. Antihypertensive food is a dietary supplement that fulfills the deficiency in the body, which is the biggest cause of hypertension.

Antihypertensive foods are often naturally obtained and used as nutraceuticals without any adulterations. **Table 2** shows some food components which is showing antihypertensive properties:

TABLE 2: ANTIHYPERTENSIVE FOOD AND THEIR FUNCTIONS

S. no.	Antihypertensive food	Function / MOA
1.	Non-roasted green coffee	Coffee or green or lightly roasted coffee is one such phytochemical which has beneficial properties to control CV health and blood pressure ²⁷
2.	Lycopene	The assumption of BP management where lycopene additive was recommended, tomato intake provided more approving results on cardiovascular risk endpoint than did lycopene supplementations ²⁸
3.	Green tea	Green tea has potent antioxidant and anti-inflammatory activities, known to conserve and enhance the endothelial function ²⁹
4.	Garlic	Garlic is effective in decreasing blood pressure in patients with unrestricted hypertension who are already on antihypertensive medications ³⁰
5.	Beet root juice	The utilization of beetroot juice on a low nitric diet as an origin of inorganic nitrate (NO ₃) may lower blood pressure ²⁸
6.	Pomegranate juice	Pomegranate may often find <i>Punica Granatum</i> constituent. <i>Punica granatum</i> L is rich in antioxidant polyphenols. e.g., ellagitannins ²⁷
7.	Dark chocolate	Cocoa is flavonoids that have been recently investigated. It is an adequate food supplement that plays a possible role in the prevention of CVD ³¹
8.	Fermented milk	Epidemiological studies suggest that people who consume more milk have a more desirable blood pressure than those who consume less milk, so dairy supplements are used as a dietary supplement to control high pressure ³²
9.	Nuts	Five large epidemiological studies have thus far; continuous consumption of nuts reduces the risk of CHD. So, it is used as a nutraceutical or as an antihypertensive food, the best known among them being the Adventist health study ³³
10.	Quercetin	Onion is a vegetable that is used in a wide variety of food in the world. It is good in a phenolic compound such as Quercetin which shows an antihypertensive effect through antioxidant properties, and it inhibits the ACE activity and Ca ²⁺ influx ³⁴

Antihypertensive Nutrients³⁵: Antihypertensive nutrients are the compounds that are naturally present in our diet with accepted nutritional levels, such as minerals, vitamins, fatty acids, and polysaccharides. Nutrients/minerals are an element

that does not maintain blood pressure but prevents the occurrence of arterial hypertension. **Table 3** shows the nutrients which are shown antihypertensive properties:

TABLE 3: ANTIHYPERTENSIVE NUTRIENTS/ MINERALS AND THEIR FUNCTIONS

S. no.	Nutrients	Functions / MOA
1.	Calcium	Calcium is often essential for bone-building or teeth, and it helps to support bone strength and plays a vital role in nerve, muscle, and glandular functions ²⁷
2.	Iron	Iron helps to assist in energy production, and it also helps to sustain and transmits the oxygen to tissue ³⁵
3.	Magnesium	Magnesium is necessary to form bone, healthy nerves, and muscle function. It may help to prohibit premenstrual problem ²⁷
4.	Phosphorous	Phosphorous is also necessary for the building of strong bones and teeth. It assists in the formulation of genetic material, storage, and production of energy ³⁵
5.	Zinc	Zinc is necessary for the cell replication; normal extension and spread in children, wound relieve production of sperm and testosterone ³⁵
6.	Flavonoids	The over 4000 flavonoids in fruit, vegetables, red wine, tea, soy, and licorice may decrease the risk factor of high blood pressure, Cerebrovascular accident, and cardiac heart disease ³⁰
7.	Omega-3 polyunsaturated fatty acids (PUFAs)	Omega-3 polyunsaturated fatty acids indicated mechanisms by which PUFAs may enhance the blood pressure control are numerous: improvement of generation and bioavailability of endothelium-derived moderately factor (NO) through up- Management and activation of endothelial NO synthase, decreased insulin- resistance, and the defeat of the renin-angiotensin-aldosterone system ³⁶
8.	Vitamins	The vitamins and ascorbate concentration in humans are conversely related to blood pressure. Especially vitamin C also appears to enhance the success of some hypertensive drugs like Amlodipine ³⁷
9.	Multivitamins	A multivitamin is a nutrient that is most extensively used as a food supplement throughout the world, and there has been a developing interest in the prospective role of multivitamins is decreasing the risk of chronic disease as well as cardiovascular disease, hypertension, cancer, and brain dysfunction ³⁸
10.	Sterols	The current analysis, which aimed to analyze the consequence of plant stanol esters on arterial stiffness and endothelial function in adults, also established no effect on measured blood pressure and also denoted antihypertensive effects of sterol despite sustained treatment for a year or more ³⁹

MATERIAL AND METHOD: A small face-to-face survey has been done on different medical shops/ drug stores in the areas of Dehradun, like near kanwali road, Dharmpur, Premnagar, Ballupur, Rispana, Doon hospital, Jogiwala. We found that some of the drug stores prefer nutraceuticals.

This survey data includes various types of nutraceuticals that are revealed through an offline (face to face) survey from December 15, 2021 to January 10, 2022. In this survey, we have collected data from chemist's responses.

Survey Report of Nutraceuticals used in Management of Hypertension: Survey is a procedure of convention data from a sample of people, regularly with the purpose of generalizing the effect to a larger population. A survey gives an analytical source of data and awareness for nearly everyone occupied in the particular's economy, from business and the media to government and academics. There are 4 modes of survey data collection: face-to-face survey, Telephone survey, Self- administered paper and pencil survey, Self-

administered computer survey. This face-to-face survey reveals which nutraceuticals are used in the market for the Management of hypertension. Nutraceuticals are often available in the market in the form of tablet; capsule and oral formulations (Syrup).

Most formulations are available in the nutraceuticals market in the form of soft gel capsules. These nutraceuticals also contain some nutrients that can decrease blood pressure, as well as the lack of nutrition in the body, such as due to lack of vitamins, calcium, and magnesium, phosphorous in the body and chronic disease due to lack of nutrients in the body. In this case, nutraceuticals or dietary supplements are also taken. This survey reveals which nutraceuticals are highly demanding in the market. As per the survey, some of the marketed formulations of nutraceuticals are as follows:

Marketed Formulations of Nutraceuticals for Hypertension: As per the survey, the marketed formulation of nutraceuticals is shown in **Table 4:**

TABLE 4: MARKETED FORMULATIONS OF NUTRACEUTICALS

Types of medicine	Marketed formulation
Tablet	Super B complex, Alpha-linolenic acid, Allvell- Z grape seed extract, Antioxidant support
Capsule	Advanced BP support, Natural formula BP Complex, Blood pressure formula, Mactotal, BP rescue, Omega fatty acids grape seed vitamins, Cardio care vegetarian capsule, Cholbiome
Liquid orals	Vegifruit syrup, Beetroot juice, Beryl tone

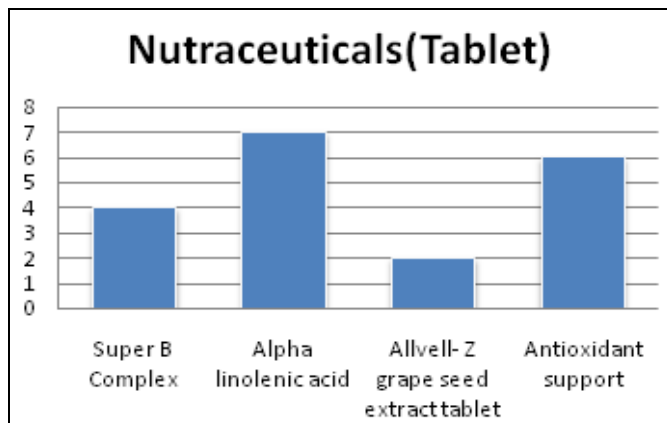


FIG. 2: GRAPH OF MARKETED DEMAND OF NUTRACEUTICALS IN THE FORM OF TABLET

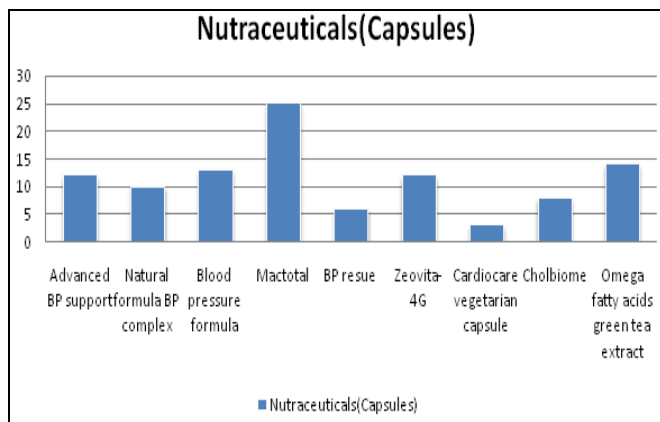


FIG. 3: GRAPH OF MARKETED DEMAND OF NUTRACEUTICALS IN THE FORM OF CAPSULE

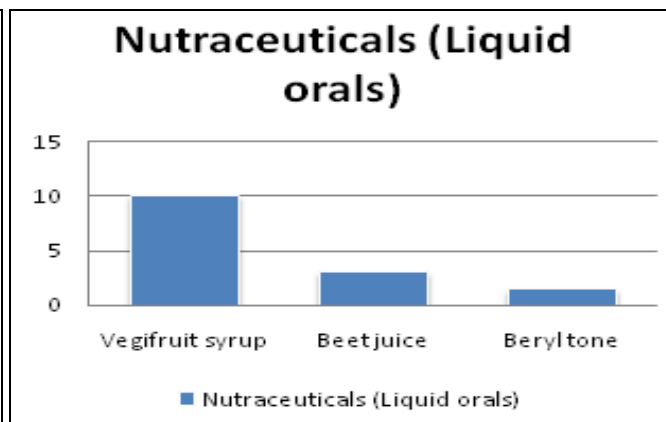


FIG. 4: GRAPH OF MARKETED DEMAND FOR NUTRACEUTICALS IN THE FORM OF LIQUID ORALS

These graphs displayed which nutraceutical is preferred for hypertension in the market and which nutraceutical is most demanding in the market. After surveying 33 drugstores, we found that the most demanding nutraceutical is Mac total. This graph shows that most preferred nutraceutical is Mactotal, and the least demanding nutraceuticals are Beryl tone and Allvell-Z grape seed extract.

Marketed Formulation, Ingredients & their Functions: These are some antihypertensive drugs that are used as a marketed formulation of nutraceuticals.

Table 5 includes the composition and the functions of these antihypertensive drugs.

TABLE 5: MARKETED FORMULATIONS OF NUTRACEUTICALS & THEIR FUNCTIONS

S. no.	Antihypertensive nutraceuticals	Composition	Functions
1	Mactotal	Omega 3 fatty acids, green tea Extract, Ginkgo biloba, Grape Seed extract, Ginseng, Vitamins, Minerals	Mactotal is used for heart-related a disease. It is a multivitamin supplement used to prevent the deficiency due to poor diet
2	Omega fatty acids, grape seed vitamins	Omega 3 fatty acids, grape seed extract, green tea extract, Ginseng grape seed, Ginkgo biloba extract, multimineral	It reduces body weight and decreases the diastolic blood pressure
3	Advanced BP support	Hawthorn extract, Hibiscus flower,	It helps to keep vessels strong and

4	Natural formula BP complex	Olive oil, Garlic, Vit.C, Niacin, Vitamin B6, B12	flexible, and it reduces the risk of heart issue
5	Blood pressure formula	Hawthorn berry, Forskohlii, Garlic, Hibiscus	It supports healthy blood pr. Levels and helps to feel better.
6	BP rescue	Wolfberry extract, Odorless garlic extract, Sage extract, Olive leaf extract, Rutin	Blood pressure formula helps to support BP levels in the normal range
7	Zeovita- 4G	Hawthorn berry, Garlic, Green tea, Coleus Forskohlii, Olive leaf	It is a blood pressure supplement that help lower and maintains blood pressure.
8	Cardiocare capsule	Omega 3 fatty acid, green tea extract, ginkgo biloba, ginseng, grape seed extract, vitamins, minerals	The antioxidants in grape seed extract can potentially protect the blood vessels from becoming damaged, which may prevent high blood pressure
9	Cholbiome	Ginkgo biloba, Lycopene, Nattokinas, Folic acid, Magnesium, Ascorbic acid	It is cardiovascular health begins with keeping the blood pressure and nerve functioning under the control
10	Lutein, glucosinolatic saponins fibers (vegifruit syrup)	Lactobacillus, Co- enzyme, L- arginine, Co- enzyme Q10	It is a CoQ10 in supplement that is purported to improve heart-related conditions like hypertension by neutralizing free radicals, increasing the production of energy in cells, and preventing the formation of blood clot
11	Beet juice	Fruit extract, vitamins, Minerals, Amino acids	This syrup affects cardiovascular risk factors such as lowering blood pressure
12	Beryl tone	Beetroot extracts, vitamins, Multimineral	It is used to help lower level of triglycerides in the blood, and high BP and to improve atheletic performance
13	Alpha-linolenic acid	Multivitamins, multimineral, lycopene, L- lysine, anti- Oxidant	This supplement prevents heart-related disease by reducing oxidative stress, and it also helps to protect cell from damage.
14	Allvell-Z grape seed extract tablet	Vitamin C& E, Glutathione, Alpha-linolenic acid	Alpha-linolenic acid is conception to decrease the risk of heart disease by helping to support normal heart rhythm and pumping
15	Antioxidant support	Grape seed extract, Vitamins, Folic acid, Manganese, Biotin	The oxidant in grape seed extract can certainly assure the blood vessels from becoming damaged, which may prevent high blood pressure
		Vitamin C, Green tea extract, Grape seed extract, Lycopene, Folic acid, Biotin	It may help to protect the cell from damage caused by free radical and it decreases the risk of high blood pressure

CONCLUSION: It is concluded that the above-studied nutraceuticals that is Mactotal, Omega fatty acids grape seed extract, Advanced BP support, Natural formula BP complex, Blood pressure formula, BP rescue, Cholbiome, Zeovita- 4G, Super B complex, Alpha-linolenic acid, Allvell-Z grape seed extract tablet, Antioxidant support, Vegifruit syrup, Beet juice, Beryl tone.

These nutraceuticals and functional foods reduce blood pressure, in which mactotal, this effect is most likely mediated by inhibiting ACE activity, modulating NO production, scavenging free radicals, and improving endothelial function. The most demanding nutraceutical is Mactotal and least demanding nutraceutical is Allvell- Z grape seed

extract and Barytone. This surveyed nutraceutical is in huge demand due to their fewer toxic effects and having good self-life as well as long life treatment with dietary foods.

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