

THE ROLE OF PHYTOSTEROLS AND PHYTOCHEMICALS IN NUTRACEUTICALS, FUNCTIONAL FOODS AND RUTFS

¹Rahul Agarwal, ²Shraddha Jaiswal

¹Assistant Professor

¹ Department of Food Technology

¹ Jaipur National University, Jaipur, India

Abstract

Food is the basic necessity of living and the body derives nutrients from it to aid in the metabolism, growth and repair. Thus, nutrients form the essential components for the basic structure of living cells. However, the availability of these components is meager, thus, at times the body requires external supply of nutrients in an artificial non-food matrix, thus, coining the term 'nutraceuticals' that provides the necessary supplements through their pharmaceutical form.

In advancement to this category, we also have functional foods that claim to operate on particular disorder or health issue through the consumption of foods that contain the functional health normalizing components. In this paper, phytosterols and phytochemicals are explained in detail. Another loaded multi-nutrient supplying category is RUTFs or Ready to Use Therapeutic Foods that are precisely used for some therapy. Thus, foods nowadays are not only meant for the survival but also as an agent that can treat or prevent disorders and provide constituents required to perform specific functions in our body.

Keywords: Nutraceuticals, Functional foods, Phytosterols, Phytosterols, RUTF

1.Introduction

Epidemiological and clinical studies have demonstrated the relationship between diet and health status. It is well known that populations consuming a large proportion of plant based foods, including fruits, vegetables, whole grains and cereals or those with a high intake of seafoods have a lower incidence of cardiovascular diseases and certain types of cancer.

The term nutraceuticals derived from 'Nutrition' and 'Pharmaceutics' in 1989 by Stephen DeFelice, MD, founder and chairman of the Foundation for Innovation in medicine (FIM), Cranford, NJ

Nutraceuticals are defined as the non-food matrix form of the complexed concentrated nutrients derived from food used to improve health and prevent diseases. Moreover a nutraceutical is any substance that is a food or a part of a food and provides medical and health benefits including the prevention and treatment of diseases.

However, nutraceuticals are products produced from foods but sold in the medicinal form of capsule, tablet, powder, solution or potion. They are not generally associated with food and have demonstrated physiological benefits and/or provide protection against chronic diseases.

2. Categories of nutraceuticals

The sources from which nutraceuticals are obtained along with the pharmacological and chemical composition categorises them. These are classified as dietary supplements, functional foods, therapeutic and pharmaceuticals.

These are presented in a non-food form usually concentrated in comparison to food and are regulated by different agencies such as FDA, however, in a manner different from drugs and foods.

2.1 Potential health benefits

Nutraceuticals have influenced substantial interests rendering to their nutritional, safety and therapeutic effects. Therefore, nutraceuticals can be used to prevent diseases, improve the immunological responses and keep aging at bay along with increasing the expected life of an individual.

These are also considered as a preventive measure for chronic diseases such as renal infections, cancers and GI disorders.

2.1.1 PHYTOSTEROLS:

They lower the cholesterol and low-density lipoproteins (LDL) concentrations. Phytosterol-deficient and high phytosterol diets which conform to recommended major macronutrient guidelines and are palatable are used in controlled feedings.

These are plant sterols (have double bond in the sterol rings) and stanols (lack a double bond in the sterol ring) that reduce the absorption, blood cholesterol concentrations and coronary heart diseases.

The therapeutic potential of naturally occurring phytosterols in diet was demonstrated by Jenkins et al. [2] that showed that a plant based diet naturally high in phytosterols considerably reduced cholesterol-LDL concentrations within a week.

These are present in the glycosylated forms in foods while the free and esterified forms are found in plants. Glycosylated forms are biologically active. The role of therapeutic diet is evaluated by comparison with the control diet that is deficient in phytosterols. 44 phytosterols are said to exist in plants. These are not produced in the body and are required from diet hence are essential for everyone.

Although being similar in function to cholesterol, their advantage is that they do not produce any side effects unlike cholesterol rich foods. Plant based diets containing phytosterols lowers serum cholesterol level (0.8 gm daily as suggested by numerous clinical trials) unlike meat or animal based diets.

Also, higher intake of plant phytosterols results in decreased risks of cancer as per epidemiological studies.

Initial results suggest that low dosage of phytosterols supplementation improve urinary tract symptoms related to the benign prostatic hyperplasia.

They function as creating a hindrance in the interaction of cholesterol with the active sites in the intestinal walls and affecting their metabolism and synthesis.

150mg of phytosterol controls absorption of cholesterol by 12%.

Determination of phytosterols:

1. Alkaline hydrolysis- standard single hydrolysis method that quantifies free and esterified phytosterols

2. Acid hydrolysis followed by alkaline hydrolysis for recovery of glycosidic phytosterols
3. Lipid derivatives are complexed to trimethylsilyl derivatives and analyzed by gas chromatography

Presence of phytosterols:

Sitosterol- 56-79%

Campesterol- 16%

Stigmasterol- 10%

Stanols- 9%

sitostanol, campestanol, avenasterol and $\Delta 5$ -avenasterol collectively contribute to 10%.

In order to get a natural supply of high amounts of phytosterols, the following foods can be included in the diet:

1. oils (wheat germ oil, rice bran oil, corn oil, canola oil),
2. seeds (sesame seed, sunflower seed),
3. nuts (pistachio, pine nut, almond),
4. whole grains such as wheat germ, bran (rice bran, corn bran, wheat bran),
5. flour (soy flour, rye flour, whole wheat flour), and soybeans

Food sources

phytosterol content (mg/100 gm)

oils:

- rice bran
- corn
- wheat germ
- flax seed
- cotton seed
- soyabean
- peanut
- olive
- coconut
- palm

vegetables:

- beet root
- brussels sprouts
- cauliflower
- onion
- carrot
- cabbage
- yam

fruits:

- orange
- banana
- apple, cherry
- peach

- 1055
- 952
- 553
- 338
- 337
- 221
- 206
- 176
- 91
- 49

- 25
- 24
- 18
- 15
- 12
- 11
- 10

- 24
- 16
- 11
- 10

2.1.1.1 METABOLISM AND BIOAVAILABILITY :

1. Absorption and metabolism of cholesterol:

Dietary cholesterol (in form of mixed micelles) $\xrightarrow{\text{cholesterol esterification}}$ absorption by enterocytes (in inner lining of intestine)

Incorporation into triglyceride-rich lipoproteins k/a chylomicrons

Circulation and depletion of triglycerides (k/chylomicron remnants)
Absorption by liver

Repackaging of cholesterol into other lipoproteins

Recirculation

Secreted into bile

Released into small intestine

2. Absorption and metabolism of dietary phytosterols:

<10% of dietary phytosterols re absorbed unlike 50-60% of cholesterol absorption [3]

Incorporation of phytosterols as mixed micelles

Absorption by enterocytes

Inhibition by activity of reflux transporters – ATP Binding Cassette Proteins (ABCG5 and ABCG8) [4]

Secretion back into the intestine at a rapid rate thus lowering absorption rate

Therefore, lower serum concentrations are achieved for phytosterols compared to cholesterol due to decreased intestinal uptake and faster excretion into bile.

MECHANISM OF ACTION:

Since no particular theories have been justified for the mechanism of phytosterols but there are many theories that are used to explain the functioning and effect of cholesterol absorption in the body.

The main belief is that absorption of cholesterol, both, produced exogenously and acquired from diet is lowered in the bloodstream due to the reduced absorption into the intestine. This is expected because of the fact that, the molecular structures of cholesterol, phytosterols a phytostanols are quite similar to each other.

Theory 1: in the presence of phytosterols and phytostanols, the cholesterol forms non-absorbable complex in the intestine which in the absence of phyto-compounds is absorbed by the lining of the intestines.

Theory 2: the cholesterol absorption occurs into the intestine after it gets fixed into the micelles like structure of the bile salts and phospholipids, however, phytosterols modify the receptors responsible for cholesterol movement.

There have been many theories that depict the absorption of cholesterol into the bloodstream and the resulting effect of phytosterol intake, however, the molecular action and their function is yet not fully understood.

Impact on Cholesterol Absorption:

Phytosterols as in form of mixed micelles decrease cholesterol absorption.

The consumption of 1.5-1.8 g/day of plant phytosterols or phytostanols reduces the cholesterol absorption in the body by 30-40%. [5][6]

With higher doses, of 2.2 g/day of plant sterols, cholesterol absorption lowers by 60%. [7]

With decreased cholesterol tissue LDL receptor expression gets enhanced resulting in increased clearance of LDL.[8]

Impact on CDH risk:

The National Cholesterol Education Programmed(NCEP) Adult Treatment Panel III has given a recommendation for the daily intake of 2 g/day of food rich in plant sterols and stanols. Also the recommended minimum dosage is 0.8-1g/day. [9]

Suggested Trials for decreased Coronary Heart Disease (CDH) risk:

1. Reduction in 10% LDL by medication or diet modification to reduce CDH risk by 20%. [10]
2. Substitution of Saturated Fats by MUFA and PUFA for 30 days results in 9% reduction of serum LDL Cholesterol [11]
3. Further, addition of 1.7 g/day of plant sterols to the same gives 24% reduction. [11]
4. Including 1g/1000 Kcal of sterol rich foods for 30 days such as peanuts, soyprotein, almonds and fibres lowers serum LDL upto 30% similar to the one induced by statin therapy (inhibits HMG-CoA reductase enzyme) [12]

Impact on Cancer risk:

As per the epidemiological studies, the increased intake of phytosterol, in particular, sitosterol reduces the risk of breast and prostate cancers. [13]

Case studies of Uruguay suggests that the intake of dietary phytosterols were much lower in people suffering from stomach, lung or breast cancer than cancer free people.[14]

Case studies of the USA shows that women affected by endometrial and breast cancers also have low dietary phytosterol intake than the non-affected ones.[15]

Intake in Benign Prostatic Hyperplasia (BPH):

BPH is the expansion of the prostate in non-cancerous condition, which causes pain in urination due to increased pressure on the urethra.

β -sitosterols (market name for plant originated Phytosterols) are used for the treatment of BPH. A review found that the intake of 130mg/day of different β -sitosterols extracts increases urinary flow by an average of 3.9 ml/ second and decrease post-residual volume by an average of 29 ml. [16]

Food Sources:

Vegetarians ,in particular, the vegans have a high content of dietary fiber in their diet, thus, have a greater uptake of phytosterols. The greatest content though is found in the unrefined oils of plant origin. Grains, legumes, nuts are also good sources.

Plant sterols or stenols are added to low-fat milk, yoghurt , mayonnaise and curd can have lower LDL uptake.

A recent meta-analysis suggested that foods such as milk, yoghurt, salad dressings , mayonnaise, etc. added with plant sterols/stenols are more effective then foods such as chocolate, orange juice, meats, cereal bars containing these phyto-compounds. [17]

Supplements:

Phytosterols as β -sterols are available in the US market without medical prescription. BPH symptoms are eliminated by the dosage of 60-130mg/day of phyto-compounds. Also, in order to control the cholesterol level in the body, soft chewing gels are also marketed that contain 0.5mg of phytosterols.

Phytosterols as an ingredient in functional foods:

Phytosterols in all food forms tested for lower serum cholesterol and LDL levels using low fat milk shoed the reduction of 16% with 1.6 g/day of phytosterol intake.

Safety:

The greatest achievement for the phytosterols and phytostanols is that they are considered Generally Recognized As Safe (GRAS) by the USFDA.(2000 and 2001)

In EU, the Scientific Committee of foods has also declared the phyto-compound's application in food products as safe for human consumption.

Legislation:

1. Europe: Novel Foods Approval(covers all European Union Countries) (2000)
2. Japan: Approved a number of enriched products(2001)
3. Australia: Novel Foods(2006) and TGA(2008) approval
4. Canada: Novel Foods Approval and Claim (2010)
5. China: Novel Food Agreement(2007)
6. Indonesia/Philippines/Thailand/Singapore/Malaysia: Novel Foods/Functional Claims/ Health Claims (2007-09)
7. India: Approved as a Food ingredient in the meeting of Scientific Panel and Scientific Committee.

3. Ready to Use Therapeutic Foods (RUTFs)

UNICEF manages acute malnutrition through the use of RUTF (ready to eat therapeutic foods).

It's the primary global procurer for RUTF and also helps other governmental and non-governmental organizations.

Another procurer of RUTF is Médecins Sans Frontières.

Clinton Foundation

Out of 20 million children suffering from acute malnutrition, 10-15% is treated using RUTF.

1.96 million children suffering from acute malnutrition were treated in 2011 alone.

However, early detection of malnutrition and its acuteness is required for effective treatment regimen through dosage of RUTF.

Benefits of RUTF:

- Safe and easy to use without medical supervision
- Cost effective
- Produced in developing countries with minimal infrastructure
- Provide all the nutrients required for recovery
- Has a good shelf life and do not spoil even after opening
- Do not require expensive packaging
- Non-water based so not infected by bacteria and stored without refrigeration
- Can be used in combination with other methods of infant and young child feeding.
- Texture is soft and crushable tasty paste like from acceptable by young children.
- Micro-organism resistant.
- Can be used directly without cooking/heating.
- Children under treatment require only a short course of basic oral medication to treat any infections for deworming, vitamin A supplementation and folic acid.
- In case of decentralized communities, about 80% of the children suffering from acute malnutrition can be successfully treated at home under proper supervision.

RUTF are energy rich foods enriched with micronutrients and used as pastes for feeding. They are soft foods and contain a homogeneous mix of lipid rich foods with a size range of less than 200µm. Primary ingredients for RUTF are:

Peanuts

Sugar

Oil

skimmed Milk powder

Vitamin- mineral supplements (CMV)

Use of RUTF is community-based management of acute malnutrition

RUTF was first introduced during the early 2000s to treat the humanitarian emergencies when access was a considerable barrier.

Its application within community management of acute malnutrition (CMAM) –strategy supported by WHO, the World Food Programme, the UNICEF and UN Standing Committee on Nutrition –has caused a sharp rise in programme coverage and as children treated successfully.[1]

In Ethiopia alone, a twelve-fold increase has been observed in the number of children treated in the past nine years.

Unlike only 9 countries in 2005, currently 61 countries have some form of treatment for severe acute malnutrition with a community component available.

Limitations of RUTF:

It is a treatment for severe acute malnutrition and not a panacea for all types of children malnutrition

In case of HIV positive children suffering from malnutrition, the effectiveness of RUTF treatment is less than HIV negative children.

Only 27% of the RUTF needs are satisfied locally with rest being imported from the advanced countries.

4.PHYTOCHEMICALS:

These are plant products that impart them color, flavor and odor and taking them in our diet also influence our bodily functions in a positive way.

The roles of phytochemicals are as:

1. Help in prevention of cancer
2. Act as antioxidants
3. Act as hormone stimulating factors
4. Prevent oxidation
5. Prevent DNA damage
6. Helps in DNA and cell repairmen
7. Stimulate the immune system

Types:

1. Carotenoids (such as beta-carotene, lycopene, lutein, zeaxanthin). Sources are Red, orange and green fruits and vegetables including broccoli, leafy greens, sweet potatoes, winter squash, apricots, cantaloupe, oranges, watermelon and tomatoes. These are useful for elimination of growth of cancer causing cells, acts as antioxidants and activates immunological responses.
2. Flavonoids (such as anthocyanins and quercetin). Sources are apples, soybeans and soya products (tofu, soy milk, edamame, etc.), coffee and tea, apple and citrus fruits. Used for inhibition of inflammation and tumor growth; may aid immunity and enhances production of such de-toxication causing enzymes.
3. Indoles and Glucosinolates(sulforaphane). These are found in vegetables such as broccoli, cabbage, collard greens, kale, cauliflower and Brussels sprouts. They causes detoxifying function of cancerous agents and limit production of cancer-related hormones, block carcinogens and prevent tumor growth.
4. Inositol(phytic acid). Found in Bran from corn, oats, rice, nuts, soybeans and soy products (tofu, soy milk, edamame, etc.), rye and wheat. They retard cancerous cell growth and acts as antioxidant.
5. Polyphenols (example are ellagic acid and resveratrol). Grapes, wine, berries, green tea, citrus fruits, apples, whole grains and peanuts. May prevent cancers, inflammation and work as antioxidants.

5. CONCLUSIONS:

The basic diet, today, does not satisfy the needs of the body for nutrition and disease resistance, thus, the extra components such as phytosterols, phytostanols and other functional foods are essentially included in the diet.

These foods do not only form a component of diet but also satisfy their specific function for which they are designed. The nutraceuticals, functional foods consisting of phyto-compounds along with Ready to Use Therapeutic Foods discussed in this paper are the key components of food today.

Therefore a daily adequate intake of these supplements containing foods may prevent human being from many types of diseases and complications.

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