A Modern Approach to Boost Health:

NUTRACEUTICALS

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Nutraceuticals are regarded as bioactive food products that provide health as-well-as medical benefits such as prevention and treatment of diseases. The need of herbal medicine is increasing day-by-day. With the modernized, competitive and stressful conditions, all types of diseases are having a field day. Allopathic cure is available for most of the diseases but they are not cost-effective and associated with a variety of side effects. Therefore, many people are inclining towards change in lifestyle and use of herbal products. These products may range from processed foods, dietary supplements, genetically engineered foods, etc. Majority of the nutraceuticals are claimed to possess multiple therapeutic benefits though substantial evidence is lacking for benefits as-well-as unwanted effects. The aim of this article is to explore and discuss the impact of nutraceuticals in healthcare based on their disease specific indications.

A. Introduction:

A nutraceutical is any substance considered as a food or its part which, in addition to its normal nutritional value provides health benefits including the prevention of disease or promotion of health.[1] Due to adverse effects of drugs, consumers are preferring food supplements to improve health. This brought revolution worldwide in the field of nutraceuticals. Nutraceuticals provide extra health benefits, in addition to the basic nutritional value found in foods. Depending on the jurisdiction, products may claim to prevent diseases, improve health, delay the ageing process, increase life-expectancy or support the structure or function of the body.

The term nutraceutical is encompassing nutrition & pharmaceutical and it was coined in 1989 by Dr Stephen L. Defelice, founder and chairman of foundation for innovation in medicine, New Jersey, USA.[2] Nutraceuticals is a broad term used to describe any product derived from food sources that provide extra health benefits along with nutritional value found in foods. [3] These products contain carbohydrates, lipids, proteins, vitamins, minerals and other necessary nutrients.[4]

The most common type of nutraceutical products are dietary supplements. A dietary supplement is a liquid or capsule version of nutrients found in foods and is taken as an additional supplement to the daily diet. Amino acids, vitamins, minerals, botanicals and herbs are all forms of dietary supplements. Amino acids help to build muscle and improve muscle function. Vitamin B_6 and B_{12} along with folic acid plays an important role in prevention of cardiovascular disease. Vitamin D strengthens bones & prevents osteoporosis and reduces certain types of cancers. Minerals such as calcium also strengthen bones and helps in prevention of osteoporosis. Herbs such as

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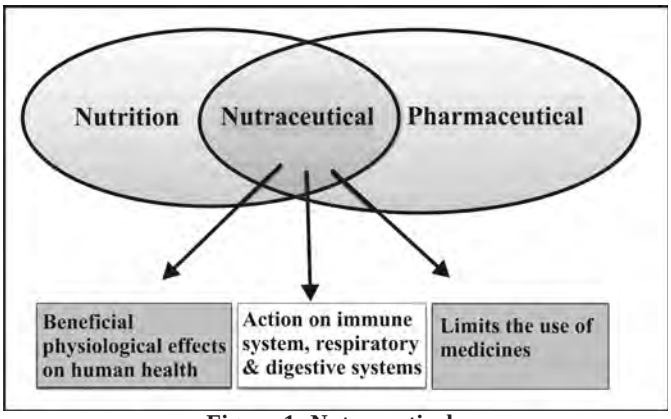

Figure-1: Nutraceuticals

St. John's wort, is used to relieve stress or depression, and also act as stimulant like tea, coffee and chocolate. Botanical dietary supplements are usually taken in the form of tea which acts as stimulant or relaxant.

Functional foods are another form of nutraceutical products. Instead of taking a dietary supplement, functional foods are enhanced with nutrients and eaten normally. The two categories of functional foods are processed food and fermented foods.

B. Health Benefits of Nutraceuticals:

From the consumers' point of view nutraceuticals offer following benefits:

- Increase the health value of our diet.
- Helps to live longer.
- Help to avoid particular medical conditions.
- May have a psychological benefit from doing something for oneself.
- May be perceived to be more "natural" than traditional medicine and less likely to produce unpleasant side-effects.
- May present food for populations with special needs (e.g. nutrient-dense foods for the elderly).

Herbal medicine constitutes an effective source of both traditional and modern medicines. According to the World Health Organization (WHO), 80 per cent of rural population depends on herbal medicine for their primary healthcare.[5] Medicinal plants though they are inadequately explored, they provide rich source of a variety of health benefits.

C. Health Benefits of Phytochemicals:

The health benefits of phytochemicals are as follows:

- Substrate for biochemical reactions.
- Cofactors of enzymatic reactions.
- Inhibitors of enzymatic reactions.
- Absorbents that bind to and eliminate undesirable constituent in the intestine.
- Scavengers of reactive or toxic chemicals.
- Enhance the absorption and / or stability of essential nutrients.
- Selective growth factor for beneficial bacteria.
- Fermentation substrate for beneficial bacteria.
- Selective inhibitors of deleterious intestinal bacteria.

D. Physiological Benefits of Nutraceuticals:

The physiological benefits of nutraceuticals are as follows:

- Cardiovascular agents,
- Anticancer agents,
- Anti-diabetics,
- Anti-obese agents,
- Chronic inflammatory disorders,
- Immune boosters, and
- Antioxidants.

E. Nutraceuticals and Diseases:

E.I. *Cardiovascular diseases*

Cardio-Vascular Diseases (CVD) is a group of disorders of the heart and blood vessels that include hypertension (high blood pressure), coronary heart disease (heart attack), cerebrovascular disease (stroke), heart failure, peripheral vascular disease, etc. It is reported that low intake of fruits and vegetables is associated with a high mortality in CVD.[6,7] Nutraceuticals in the form of antioxidants, dietary fibers, omega-3 Poly-Unsaturated Fatty Acids (ω-3 PUFAs), vitamins, and minerals are recommended together with physical exercise for prevention and treatment of CVD. It has been demonstrated that the molecules like polyphenols present in grapes and in wine alter cellular metabolism and signaling, which is consistent with reducing arterial disease.[8]

Nutraceuticals, vitamins, antioxidants, minerals, weight reduction, exercise, cessation of smoking and restriction of alcohol & caffeine plus other lifestyle modifications can prevent, delay the onset, reduce the severity, treat, and control hypertension. Nutrients and nutraceuticals with calcium channel blocking activity (thus antihypertensive activity) include α-lipoic acid, magnesium, Vitamin B_6 (pyridoxine), Vitamin C, N-acetyl cysteine, Hawthorne, Celery, ω-3 fatty acids, etc.[9] Flavonoids, present in

onion, endives, cruciferous vegetables, black grapes, red wine, grapefruits, apples, cherries and berries[10], play a major role in curing CVD.[11,12] Flavonoids block the Angiotensin-Converting Enzyme (ACE) that raises blood pressure (BP); by blocking the enzyme cyclo-oxygenase that breaks down prostaglandins, which prevent platelet stickiness and, hence, platelet aggregation.

Cholesterol is a major significant risk factor in CVD. Sterols occur in most plant species and are called as phytosterols. Green and yellow vegetables contain significant amounts and their seeds' concentrate the sterols. Phytosterols compete with dietary cholesterol by blocking the uptake as-well-as facilitating its excretion from the body. Phytosterols in diet have the potential to reduce the morbidity and mortality from CVD.[13] Milk and eggs are important animal sources of nutraceuticals like proteins and polyunsaturated fats or Essential Fatty Acids (EFAs). EFAs are required for production and rebuilding of cells, to reduce BP, lower cholesterol and triglycerides, reduce the risk of blood clots, help prevent many diseases including arthritis, arrhythmias, and other CVDs.[14] Nutritional value of egg is increased because of added Gamma Linolenic Acid (GLA) which has many benefits, including prevention and management of CVD like hypertension.[15]

Fatty acids present in fish such as ω-3 series (ω-3 fatty acids) are well-established dietary components affecting plasma lipids and the major cardiovascular disorders, such as arrhythmias.[16,17]

E.II. *Cancer*

Cancer has emerged as a major public health problem in developing countries, matching the industrialized nations. A healthy lifestyle and diet can help in preventing cancer.[18,19] People who consume large amounts of lutein-rich foods such as chicken eggs, spinach, tomatoes, oranges and leafy greens experienced the lowest incidence of colon cancer.[20] Chronic inflammation is associated with a high cancer risk. At the molecular level, free radicals and aldehydes, produced during chronic inflammation, can induce deleterious gene mutation and post-translational modifications of key cancer-related proteins. Chronic inflammation is also associated with immune suppression, which is a risk factor for cancer.

Ginseng acts as anti-inflammatory molecule that targets many of the key players in the inflammation-to cancer sequence.[21] Recently, attention has been on phytochemicals that possess cancer-preventive properties. Besides chemopreventive components in vegetables and fruits, some phytochemicals derived from herbs and spices also have potential anticarcinogenic and antimutagenic activities, among other beneficial health effects. A broad range of phyto-pharmaceuticals with a claimed hormonal activity, called "phyto-estrogens", is recommended for prevention of prostate / breast cancer.[22] Tannins also called proanthocyanidins, detoxify carcinogens and scavenge harmful free radicals.[23] Tannins in cranberries also protect against urinary tract infections. It is present in blackberries, blueberries, cranberries, grapes, lentils, tea and wine. Ellagic acid is a proven anti-carcinogen[24] which is used in alternative medicine and to prevent cancer.[25] It is present in strawberries, cranberries, walnuts, pecans, pomegranates and the best source, red raspberry seeds. Phenolics such as ferulic, caffeic & gallic acids and curcumin are reported to possess anticancer activity.[26]

Cruciferous vegetables broccoli, cauliflower, cabbage, watercress, rape seed oil and mustard possess glucosinolates that acts as powerful activators of liver detoxification enzymes.[27]

High intake of cruciferous vegetables, glucosinolates and their hydrolysis products, including indoles and isothiocyanates has been associated with lower risk of lung and colorectal cancer. They also regulate white blood cells and cytokines.

Curcumin is a polyphenol derived from the plant *Curcuma longa*, commonly called turmeric. Curcumin was reported to possess anticarcinogenic, antioxidative and anti-inflammatory properties.[28,29] The anticancer potential of curcumin stems from its ability to suppress proliferation of a wide variety of tumor cells. Beet roots, cucumber fruits, spinach leaves, and turmeric rhizomes, were reported to possess antitumor activity.[30]

E.III. *Diabetes*

Diabetes mellitus is characterized by abnormally high levels of blood glucose, either due to insufficient insulin production, or due to its ineffectiveness. The most common forms of diabetes are type I diabetes (5%), an autoimmune disorder; and type 2 diabetes (95%), which is associated with obesity. Gestational diabetes occurs in pregnancy.[31] Diabetes, like most chronic health conditions, not only places substantial economic burdens on society as a whole but also imposes considerable economic burdens on individual patients and their families. Diet therapy is the cornerstone for the management of gestational diabetes mellitus. The use of herbal dietary supplements are believed to benefit type 2 diabetes mellitus; however, few have been proven to do so in properly designed randomized trials.

Isoflavones are phytoestrogens; they have a structural / functional similarity to human estrogen and have been consumed by humans worldwide. Of all phytoestrogens, soy isoflavones have been studied the most. A high intake of isoflavone (20-100 mg/day) is associated with lower

incidence and mortality rate of type II diabetes, heart disease, osteoporosis and certain cancers.[32]

ω-3 fatty acids have been suggested to reduce glucose tolerance in patients predisposed to diabetes. For the synthesis of the long chain ω-3 fatty acids, insulin is required; the heart may, thus, be particularly susceptible to their depletion in diabetes. Ethyl esters of ω-3 fatty acids may be potentially beneficial in diabetic patients.[33]

Docosahexaenoic acid modulates insulin resistance and is also vital for neurovisual development. This is especially important in women with gestational diabetes mellitus which foster the recommendation for EFAs during pregnancy.[34]

Dietary intake of magnesium reduces diabetes risk and improves insulin sensitivity. Chromium picolinate, calcium and vitamin D are reported to promote insulin sensitivity and improve glycemic control in some diabetics; extracts of bitter melon and of cinnamon have the potential to treat and possibly prevent diabetes. However it has been suggested that nutraceuticals with meaningful doses of combinations may substantially prevent and presumably could be marketed legally.[35]

E.IV. *Obesity*

Obesity is a global public health problem and is defined as accumulation of unhealthy amount of body fat. It is a well-established risk factor for many disorders like angina pectoris, congestive heart failure (CHF), hypertension, hyperlipidemia, respiratory disorders, renal vein thrombosis, osteoarthritis, cancer, reduced fertility, etc.[36]

One of the primary causes for rapid rise in obesity rates is the increased availability of high-fat and energy dense foods.[37] Excessive consumption of energy-rich foods such as snacks, processed foods and soft drinks can encourage weight gain, which calls for a limit in the consumption of saturated and trans-fats apart from sugars and salt in the diet. Physical exercise and restricted intake of high calorie food have been shown to be only moderately successful in managing obesity. Thus, many healthcare practitioners and obese individuals are seeking the help of pharmaceuticals and nutraceuticals to treat obesity.

Table 1: Classification of Nutraceuticals Based Upon Food Source[53]

Food Source	Examples
Plants	β-glucan, Ascorbic acid, γ-tocotrienol, Quercitin, Luteolin, Cellulose, Leutin, Gallic acid, Perillyl alcohol, Indole-3-carbonol, Pectin, Daidzein, Glutathione, Potassium, Allicin, δ-limonene, Genestein, Licopene, Hemicellulose, Lignin, Capsaicin, Geraniol, β-ionone, α-tocopherol, β-carotene, Nordihydro capsaicin, Selenium, Zeaxanthin, Minerals.
Animals	Conjugated Linoleic Acid (CLA), Eicosa Pentaenoic Acid (EPA), Docosa Hexenoic Acid (DHA), Spingolipids, Choline, Lecithin, Calcium, Coenzyme Q10, Selenium, Zinc, Creatinine, Minerals.
Microbes	*Saccharomyces boulardii* (yeast), *Bifidobacterium bifidum, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus acidophilus* (LCI), *L. acidophilus* (NCFB 1748), *Streptococcus salvarius.*

A tolerable and effective nutraceutical that can increase energy expenditure and / or decrease caloric intake is desirable for body weight reduction. Herbal stimulants such as ephedrine, caffeine, chitosan and green tea have proved effective in facilitating body weight loss.[38-41] However, their use is controversial due to their ability to cause undesired effects. Buckwheat seed proteins have beneficial role in obesity and constipation acting similar to natural fibers present in food. 5-hydroxytryptophan decreases weight loss and green tea extract increases the energy expenditure that may promote weight loss.[42\

E.V. *Inflammatory disorders*

Inflammation is the response of body tissues to injury or irritation, characterized by pain & swelling, redness and heat. Arthritis is a general term that describes inflammation in joints. Some types of arthritis associated with inflammation include: rheumatoid arthritis shoulder tendinitis or bursitis gouty arthritis and polymyalgia rheumatica. Micronutrients for which preliminary evidence of benefit exists include vitamin C and vitamin D. In addition, numerous nutraceuticals that may influence osteoarthritis pathophysiology, including glucosamine, chondroitin, sadenosylmethionine, ginger and avocado / soybean unsaponifiables, have been tested in clinical trials. These products are safe and well-tolerated, but interpretation of the collective results is hampered by heterogeneity of the studies and inconsistent results.[43]

Cat's claw acts as a potent anti-inflammatory agent. The two known species of cat's claw are Uncaria guianensis, used traditionally for wound healing; and Uncaria tomentosa, which has numerous medicinal uses & is most commonly found in supplements. Cat's claw is a rich source of phytochemicals 17 alkaloids, glycosides, tannins, flavonoids, sterol fractions and other compounds.[44] Scientists previously attributed the efficacy of cat's claw to compounds called oxindole alkaloids; more recently, however, water-soluble cat's claw extracts that do not contain significant amounts of alkaloids were found to possess strong antioxidant and anti-inflammatory effects that are independent of their alkaloid content.[45,46]

E.VI. *Immune boosters*

Nutrients present in the diet play a crucial role in maintaining an "optimal" immune response, on the organism's immune status and susceptibility to a variety of disease conditions. A wide range of phyto-pharmaceuticals with a claimed hormonal activity, called "phyto-estrogens", is recommended for prevention of various hormonal imbalance diseases. In this respect, there is a renewed interest in soy isoflavones (genistein, daidzein, biochanin) as potential superior alternatives to the synthetic Selective Estrogen Receptor Modulators (SERMs), which are currently applied in hormone replacement therapy. Phytochemicals integrate hormonal ligand activities and interfere with signaling cascades; their therapeutic use may not be restricted to hormonal ailments only, but may have applications in cancer chemoprevention and / or certain inflammatory disorders as well.[47]

Nutraceuticals that belong to the category of immune boosters and / or antiviral agents are useful to improve immune function and accelerate wound-healing. They include extracts from the coneflowers, or herbs of the genus Echinacea, such as *Echinacea purpurea*, *Echinacea angustfolia*, *Echinacea pillida*, and mixtures thereof; extracts from herbs of the genus Sambuca, such as elderberries; and Goldenseal extracts. The coneflowers root extract contains varying amounts of unsaturated alkyl ketones or isobutylamides. Goldenseal is an immune booster with antibiotic activity, and includes compounds like berberine and hydrastine, which stimulate bile secretion and constrict peripheral blood vessels respectively. *Astragalus membranaceous*, *Astragalus mongolicus*, and other herbs of the genus Astragalus are also effective immune boosters in both natural and processed forms. Astragalus stimulates development and transformation of stem cells in the marrow and lymph tissue to active immune cells.

The effect of plant and bacteria on systemic immune and intestinal epithelial cell function has led to new credence for the use of probiotics and nutraceuticals in the clinical setting. The probiotics have been found to be effective in conditions like infectious diarrhoea in children and recurrent *Clostridium difficile* induced infections. Evidence is being acquired for the use of probiotics in other gastrointestinal infections, irritable bowel syndrome and inflammatory bowel disease.[48]

Supplementation with probiotics may provide maturational signals for the lymphoid tissue and improve the balance of pro- and anti-inflammatory cytokines. Dietary nucleotides may improve growth and immunity; optimize maturation, recovery and function of rapidly dividing tissue.[49]

Usage of probiotics in the treatment of specific diseases possesses ability to reduce antibiotic use. Most probiotic preparations are comprised of one or more Lactic Acid Bacteria (LAB). Within this

Table 2: Classification of Nutraceuticals Based Upon Mechanism of Action[53]

Anticancer	Positive Influence on Blood Lipid Profile	Antioxidant Activity	Anti-Inflammatory	Osteogenetic (Or) Bone Protective
Capsaicin	β-glucan	CLA	Linolenic acid	CLA
Genestein	γ-tocotrienol	Ascorbic acid	EPA	Soy protein
Daidzein	α-tocotrienol	β-carotene	DHA	Genestein
α-tocopherol	MUFA	Polyphenolics	GLA	Daidzein
γ-tocotrienol	Quercetin	Tocopherols	Capsaicin	Calcium
Conjugated Linoleic acid	ω-3 PUFA	Tocotrienols	Quercetin	Casein phosphopeptides
Lactobacillus acidophilus	Reseveratrol	Indole-3-carbonol	Curcumin	FOS (Fructo-Oligo Saccharides)
Sphingolipids	Tannins	α-tocopherol		Inulin
Limonene	β-sitosterol	Ellagic acid		
Diallyl sulphide	Saponins	Lycopene		
Ajoene	Guar	Lutein		
α-tocotrienol	Pectin	Glutathione		
Enterolactone		Hydroxytyrosol		
Glycyrrhizin		Luteolin		
Equol		Oleuropein		
Curcumin		Catechins		
Ellagic acid		Gingerol		
Lutein		Chlorogenic acid		
Carnosol		Tannins		
L. bulgaricus				

Table 3: Classification of Nutraceuticals Based on Chemical Nature[53]

Class / Components	Source	Potential Benefits
Carotenoids		
Alpha carotene	Carrots	Neutralizes free radicals which may cause damage to cells
Beta carotene	Various fruits, vegetables	Neutralizes free radicals
Lutein	Green vegetables	Health vision
Lycopene	Tomatoes & tomato products	Reduces risk of prostate cancer
Zeaxanthin	Eggs, citrus, corn	Health vision
Collagen hydrolysate		
Collagen hydrolysate	Gelatine	Improves some symptoms associated with osteoarthritis
Dietary fibre		
Insoluble fibre	Wheat bran	Reduce risk of breast and colon cancer
Beta glucan	Oats	Reduces risk of CVD
Soluble fibre	Psyllium	Reduces risk of CVD
Whole grains	Cereal grains	Reduces risk of CVD
Fatty acids		
Omega-3 fatty acids - DHA / EPA	Tuna, fish & marine oils	Reduces the risk of CVD & improves mental, visual functions
CLA	Cheese, meat products	Improve body composition, may decrease risk of certain cancers
Flavanoids		
Anthocyanidins	Fruits	Neutralises free radicals, may reduce the risk of cancer
Catechins	Tea	Neutralises free radicals, may reduce the risk of cancer
Flavanones	Citrus	Neutralises free radicals, may reduce the risk of cancer
Flavones	Fruits / vegetables	Neutralises free radicals, may reduce the risk of cancer
Glucosinolates, Indoles, Isothiocyanates		
Sulforaphane	Cruciferous vegetables (Broccoli, Kale), Horse raddish	Induces detoxification enzymes, may reduce the risk of cancer
Phenols		
Caffeic acid	Fruits, vegetables, citrus	Antioxidant like activities, may reduce the risk of degenerative diseases, heart diseases & eye disesases
Plant sterols		
Stanol ester	Corn, soy, wheat, wood oils	Lowers blood cholesterol by inhibiting cholesterol absorption
Prebiotics / Probiotics		
Fructo-Oligo Saccharides (FOS)	Jerusalem artichokes, shallots, onion powder	May improve gastro-intestinal health
Lactobacillus	Yogurt, other diary	May improve gastro-intestinal health
Saponins		
Saponins	Soybeans, soy foods, soy protein containing foods	May lower LDL cholesterol; anticancer activity
Soy Protein		
Soy protein	Soybeans, soy-based foods	25 gm per day may reduce risk of heart disease
Phytoestrogens		
Isoflavones / Daidzein, Genistein	Soybeans, soy-based foods	May reduce menopause symptoms, such as hot flashes
Lignans	Flax, rye, vegetables	May protect against some cancers and heart diseases
Sulfides / Thiols		
Diallyl sulphide	Onions, garlic, leeks, scallions	Lowers LDL cholesterol, maintains healthy immune system
Allyl methyl trisulfide, Dithiol thiones	Cruciferous vegetables	Lowers LDL cholesterol, maintains healthy immune system
Tannins		
Proanthocyanidins	Cranberries, cranberry products, cocoa, chocolate	May improve urinary tract health; may reduce risk of CVD

group, strains of Lactobacillus, Bifidobacterium and occasionally Streptococcus are most commonly used.[50,51] A supplementary use of oral digestive enzymes and probiotics is also an anticancer dietary measure towards decreasing the incidence of breast, colon-rectal, prostate and bronchogenic cancer.[52]

F. Conclusion:

Nutraceuticals are present in most of the food ingredients with varying concentration. Concentration, time and duration of supply of nutraceuticals influence human health. Manipulating the foods, the concentration of active ingredients can be increased. Diet rich in nutraceuticals along with regular exercise, stress reduction and maintenance of healthy body weight will maximize health and reduce disease risk.

Many industries manufacture and market nutraceuticals, where the side effects (especially consumed in large quantities) of these nutraceuticals are not reported or often unproven. In order to have scientific knowledge about nutraceuticals, public should be educated where recommended daily doses of these nutraceuticals should be known by each consumer. With the rapidly increasing interest in the nutraceutical revolution, there is a need to establish a vibrant nutraceutical research community which is absolutely necessary to convert majority of potential nutraceuticals to established ones, thereby, truly delivering their enormous benefits.

G. Abbreviations:

ω-3 = Omega-3. *ACE* = Angiotensin-Converting Enzyme. *BP* = Blood Pressure. *CHF* = Congestive Heart Failure. *CLA* = Conjugated Linoleic Acid. *CVD* = Cardio-Vascular Disease. *DHA* = Docosa Hexenoic Acid. *EFA* = Essential Fatty Acid. *EPA* = Eicosa-Pentaenoic Acid. *FOS* = Fructo-Oligo Saccharide. *GLA* = Gamma Linolenic Acid. *LAB* = Lactic Acid Bacteria. *LDL* = Low Density Lipo-proteins. *PUFA* = Poly-Unsaturated Fatty Acid. *SERM* = Selective Estrogen Receptor Modulator. *WHO* = World Health Organization.

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