

A Review - Nutraceutical and their applications in diseases

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ABSTRACT

In this era of novel technological innovations, human beings have adopted such a changed lifestyle where food intake is devoid of adequate beneficial nutrients. This problem resulted in increased risk of systemic diseases like diabetes, in apoptosis and disease, Alzheimer's disease, osteoarthritis, cardiovascular and various other lifestyle diseases and as remedy, pharmaceutical drugs are prescribed, which, by default, come with adverse effects and complications. To overcome this, researchers have come up with the concept of nutrients as medicines that has given rise to a self-explanatory term called "nutraceuticals". The word 'nutraceutical' consists of two basic elements- "nutrition" and "pharmaceutical". Nutraceuticals, in broad sense, are food or part of food that provide medicinal or health benefits along with their basic nutritional value. Its benefits also include the prevention and treatment of diseases with hardly any side effect or toxicity. The different food products known as nutraceuticals are dietary fibre, prebiotics, probiotics, polyunsaturated fatty acids (PUFA), antioxidants and other different types of herbal/ natural foods. Since nutraceuticals play a significant role in combating some of the major health issues, this review article is an attempt to highlight the role of nutraceuticals in modifying and maintaining normal physiological functions that maintain an overall well-being of human health.

Keywords: -Prebiotic, Probiotic, Polysaturated fatty acids, Antioxidants

I. INTRODUCTION

According to Ayurveda "When diet is incorrect, medicine is of no use; when diet is correct, medicine is of no need". The shifting of people towards a positive approach of prevention of ailments when people stay healthy and fit. Moreover, consumers are overburdened due to expensive, the advanced ailment treatment and prevention by the use of ayurvedic medicine. Thus, it requires to standardize the functional component of food to maintaining well-being, modulating immunity and protection against different types of ailments. Firstly the name nutraceuticals was used by Stephen DeFelicety defined the food or parts of food that gives beneficial affects, and also gives medical benefits which helps in treatment of different ailments^[1]

Hippocrates (460-377 BC) is known as the Father of modern medicine. He stated "Let food be thy medicine and medicine be thy food", to predict the relationship between appropriate foods and health and their therapeutic benefits. Nutraceuticals are isolated nutrients, herbal products, dietary supplements, and diets. Nutraceuticals not cause side effects generally nutraceuticals are non toxic in nature. The word nutraceutical is derived from two words nutrients and pharmaceutical.

II. CLASSIFICATION

1. Based on chemical constituents

Vitamin A, K, E, C,	Vitamin B1, B2, B3, B6	Folic acids
Calcium	Iron	Magnesium
Phosphorus, chromium	Cobalt, Copper	Iodine

2. Herbs or botanical

Herbal (botanicals source)	Therapeutic activity
Aloe Vera gel (Aloe Vera L. N.L.Burm.)	Dilates capillaries, anti-inflammatory, emollient, wound healing properties
Ephedra (Ephedra sinica Stapf.)	Bronchodilator, vasoconstrictor, reduces bronchial Edema
Garlic (Allium sativum L)	Antibacterial, antifungal, antithrombotic, hypotensive antiinflammatory
Licorice (Glycyrrhiza glabra L.)	Expectorant, secretolytic, treatment of peptic ulcer
Ginger (Zingiber officinale Rosc.)	Carminative, antiemetic, cholagogue, positive inotropic

3. Dietary supplements

Ketogenic diets	Minimally refined grains	Several species of edible mushrooms
Glucosamine sulphate	Peptides/Hydrolates	Dairy foods
Phytoestrogens	Chondroitin sulphate	Vitamins

4. Based on diseases

Diabetes	Obesity	Cancer
Anti – inflammatory activities	Allergy	Alzheimer’s disease
Vision improving agents	Osteoarthritis	Cardiovascular disease

[2,3]

NUTRACEUTICAL AND DISEASES

Diabetes

The cases of diabetes are increasing, mostly in countries that are developing. The Diabetes increased due to obesity and due to less physical activity, incorrect intake of nutrients and foods, the biggest reason of growth of diabetes in developing countries is wrong lifestyle. It is estimated that worlds 9.3% population faces Diabetes in very short time in future.

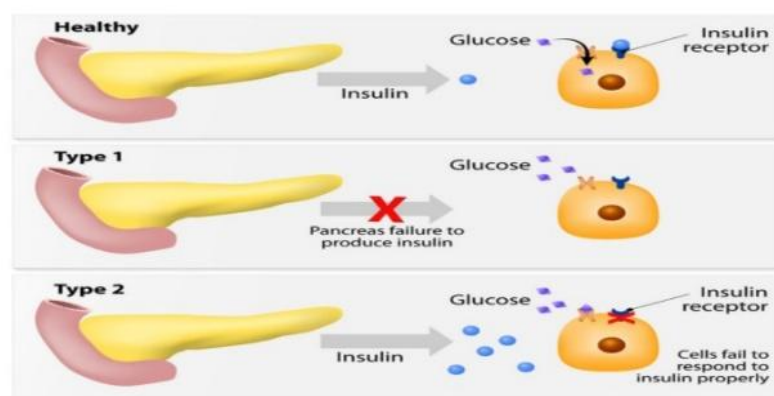
Diabetes mellitus is derived from the Greek word diabetes, meaning siphon – to pass through and the Latin word mellitus meaning sweet. A review of the history shows that the term “diabetes” was first used by Apollonius of Memphis around 250 to 300 BC. Ancient Greek, Indian, and Egyptian civilizations discovered the sweet nature of urine in this condition, and hence the propagation of the word Diabetes Mellitus came into being. Mering and Minkowski, in 1889,

discovered the role of the pancreas in the pathogenesis of diabetes. In 1922 Banting, Best, and Collip purified the hormone insulin from the pancreas of cows at the University of Toronto, leading to the availability of an effective treatment for diabetes in 1922. Over the years, exceptional work has taken place, and multiple discoveries, as well as management strategies, have been created to tackle this growing problem. Unfortunately, even today, diabetes is one of the most common chronic diseases in the country and worldwide. In the US, it remains as the seventh leading cause of death.

Diabetes mellitus (DM) is a metabolic disease, involving inappropriately elevated blood glucose levels. DM has several categories, including type 1, type 2, maturity-onset diabetes of the young (MODY), gestational diabetes, neonatal diabetes, and secondary causes due to endocrinopathies, steroid use, etc. The main subtypes of DM are Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM), which classically result from defective insulin secretion (T1DM)

Figure 1 Types of Diabetes Mellitus

DIABETES MELLITUS



And/or action (T2DM). T1DM presents in children or adolescents, while T2DM is thought to affect middle-aged and older adults who have prolonged hyperglycemia due to poor lifestyle and dietary choices.^[9]

Globally, over ~500 million people have type 2 diabetes (T2D) and another ~500 million have impaired glucose tolerance, in part due to poor nutrient intake.^[5]

The T2D prevalence is one of the highest in Europe. On the other hand, in India, for instance, where the population is largely vegetarian, relying on cereals for their diet, the obesity incidence is also steadily increasing. It is estimated that India will have approximately 80 million people with diabetes by 2030, leaving China (~45 million) and the USA (~35 million) behind by a significant margin.^[6,7]

Etiology

In the islets of Langerhans in the pancreas, there are two main subclasses of endocrine cells: insulin-producing beta cells and glucagon secreting alpha cells. Beta and alpha cells are continually changing their levels of hormone secretions based

on the glucose environment. Without the balance between insulin and glucagon, the glucose levels become inappropriately skewed. In the case of DM, insulin is either absent and/or has impaired action (insulin resistance), and thus leads to hyperglycemia.

T1DM is characterized by the destruction of beta cells in the pancreas, typically secondary to an autoimmune process. The result is the absolute destruction of beta cells, and consequentially, insulin is absent or extremely low.

T2DM involves a more insidious onset where an imbalance between insulin levels and insulin sensitivity causes a functional deficit of insulin. Insulin resistance is multifactorial but commonly develops from obesity and aging.

The genetic background for both types is critical as a risk factor. As the human genome gets further explored, there are different loci found that confer risk for DM. Polymorphisms have been known to influence the risk for T1DM, including major histocompatibility complex (MHC) and human leukocyte antigen (HLA).^[8]

Categories of nutraceuticals and their role in diabetes

Dietary supplements: Reagents derived from other sources (e.g. pyruvate, chondroitin sulphate, steroid

hormone precursors) serving specific functions, such as sports nutrition, weight-loss supplements and meal replacements.

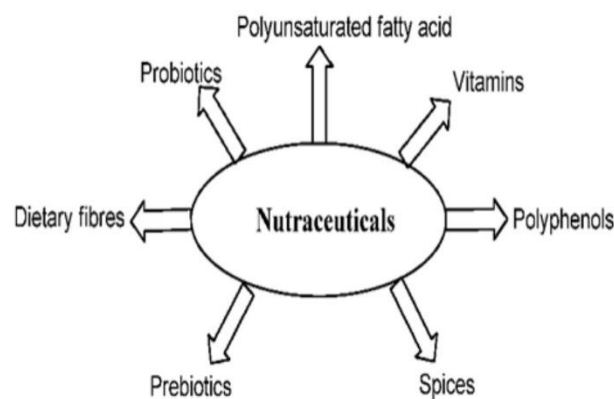


Figure 2 Diabetes Preventive Nutraceutical

The purpose of this review is to discuss these issues and provide a methodological framework for the clinical investigation of nutraceuticals in diabetes mellitus and metabolic syndrome.

Antioxidant of vitamins Animal studies have shown that an adequate supply of dietary antioxidants may prevent or delay diabetes complications including renal and neural dysfunction by providing protection against oxidative stress^[10].

Vitamin C (ascorbic acid) is a chain-breaking antioxidant, Scavenging ROS directly, and preventing the propagation of Chain reactions that would otherwise lead to a reduction in protein Glycation.¹⁸ In animals, vitamin C also reduces diabetes-induced Sorbitol accumulation and lipid peroxides in erythrocytes. Vitamin C (800 mg/day) partially replenishes vitamin C levels in patients with Type 2 DM and low vitamin C levels but does not improve endothelial dysfunction or insulin resistance^[11].

Vitamin E

Vitamin E is an essential fat soluble vitamin and functions primarily as an antioxidant. Low levels of vitamin E have been Associated with increased incidence of diabetes and some research Suggests people with diabetes have decreased levels of antioxidants. Additional evidence indicates that people with diabetes may also have greater anti-oxidant requirements, due to increased

free radical Production secondary to hyperglycaemia. Doses of vitamin E up to 400 IU are generally believed to be safe. Doses over 800 IU may Alter blood clotting although supplement trials that have monitored Prothrombin times in subjects have noted no increases^[12,13].

Carbohydrates

Carbohydrates are the energetic substrate related to the greatest Impact on glycaemia levels. The total amount of carbohydrates is the main factor responsible for the post-prandial response, but there are other variables, such as type of carbohydrate, richness in fibre, the way of cooking, degree of maturity, etc., Moreover, there are other factors that can also influence post-prandial Glycaemia such as pre-prandial glycaemia, macronutrient distribution Of the whole meal (fats and proteins) and the hypoglycaemic treatment Administered: oral tablets or insulin^[14].

Anti-diabetic claims of herbs

By virtue of richness in essential phytonutrients, ayurvedic Herbs may help as “Potentiators” for these drugs and play a supportive role. There is vast potential of selected medicinal plants from Ayurveda and Indian folk Role medicine. Several works have been attempted by CSIR, ICMR, DBT, and academia on role of herbal nutraceuticals, nutritionals and Naturals in metabolic disorders like diabetes.^[15, 16]

Table1.Name of the plant reported mechanism of action

Acacia arabica (Lam.) Muhl. Common name: Babul [Family: Fabaceae]	Acts through release of insulin from pancreatic beta cells, which accounts for the hypoglycaemic activity (Singh, 1975; Wadood, 1989)
Aegle marmelos (L.) Correa Common name: Wood apple [Family: Rutaceae]	Increases utilization of glucose; either by direct stimulation of glucose uptake or via the mediation of enhanced insulin secretion and also decreases the elevated glucose and glycosylated haemoglobin levels (Kamalakkanan, 2003)
Allium cepa L. Common name: onion [Family: Liliaceae]	Lowers blood glucose level and has potent antioxidant activity, which may account for the hypoglycaemic potential (Augusti, 1973)
Aloe vera (L.) Burm.f. Common name: Aloe [Family: Aloaceae]	Maintains glucose homeostasis by controlling the carbohydrate metabolizing enzymes and stimulates insulin release from pancreatic beta cells (Ajabnoor, 1990)
Annona squamosa L. Common name: Sugar apple [Family: Annonaceae]	Lowers blood glucose level (Shirwaikar, 2004)
Artemisia pallens Wall. Ex DC. Common Name: Davana [Family: Compositae]	Inhibits glucose re-absorption or increase in peripheral glucose utilization (Subramaniam, 1996)
AzadirachtaindicaA.Juss. Common name: Neem [Family: Meliaceae]	Inhibits action of epinephrine on glucose metabolism, resulting in increased utilization of peripheral glucose and exhibits hypoglycaemic activity without altering the serum cortisol concentration (Chattopadhyay, 1999; Gholap and Kar, 2004)
Caesalpinia bonducella (L.) Roxb. Common name: Chinese Cinnamon [Family: Caesalpiniaceae]	Increases the release of insulin from pancreatic cells (Sharma, 1997)
Morus alba L. Common name: White mulberry [Family: Moraceae]	Acts by increasing glucose uptake (Chen, 1995).
Punica granatum L. Common name: Pomegranate [Family: Punicaceae]	Inhibits intestinal alpha-glucosidase activity, leading to anti-hyperglycaemic property (Li, 2005)
Ocimum sanctum L. Common name: Holy Basil [Family: Lamiaceae]	Acts by cortisol inhibiting potency (Gholap, 2004)
Murrayakoenigii (L.) Spreng. Common name: curry-leaf tree [Family: Rutaceae]	Increases glycogenesis and decreases glycogenolysis and gluconeogenesis (Khan, 1995)
Coccinia indica Wight & Arn. Common name: Ivy gourd [Family: Cucurbitaceae]	Suppresses glucose synthesis, through depression of the key gluconeogenic enzymes glucose-6- Phosphatase and fructose-1, 6-bisphosphatase and enhances glucose oxidation by shunt pathway through Activation of its principal enzyme glucose- 6-phosphate. Also has an insulin secretagogue effect and acts Like

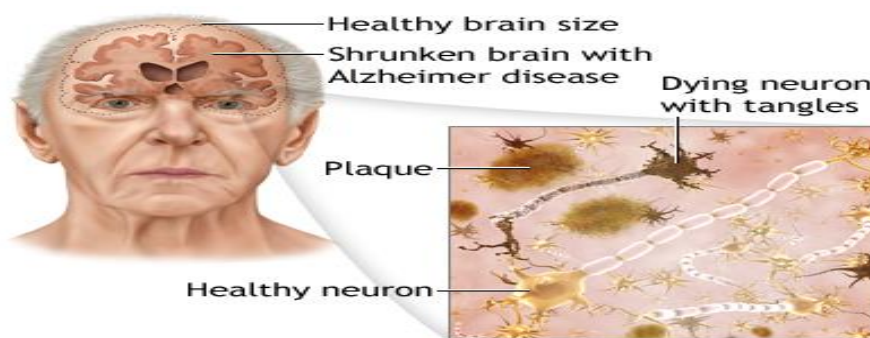
	insulin by correcting elevated enzymes in glycolytic pathway (Kamble, 1998)
Helicteresisora L. Common name: Screw tree[Family: Sterculiaceae]	Acts through insulin-sensitizing activity (Chakrabarti, 2002)
Ipomoea batatas (L.) Lam. Common name: Sweet potato[Family: Convolvulaceae]	Reduces insulin resistance and possibly acts by maltase inhibition (Matsui, 2002)
Enicostemmalittorale Blume Common name: Nahi[Family: Gentiaceae]	Enhances glucose-induced insulin release from isolated rat pancreatic islets, mediated through K (+)-ATP channel-dependent pathway (Maroo, 2002)
Catharanthusroseus (L.) G. Don Common name: Madagaskarperiwinkle [Family: Apocynaceae]	Increases metabolism of glucose and enhances secretion of insulin either from the beta cells of Langerhans or through extra pancreatic mechanism (Nammi, 2003)

Nutraceuticals against Alzheimer’s Disease (AD)^[17]

Senile Dementia Alzheimer’s (SDAT) is also known as Alzheimer’s Disease (AD), the most common type of dementia Primary

degenerative dementia of the Alzheimer’s type (PDDAT) or simply Alzheimer’s, there are different types of nutraceuticals are used in the prevention and possible treatment of Alzheimer’ s disease.

Figure 3. How Alzheimer’s disease affects Our Brain



Antioxidants

Antioxidants play most important role in nearly all diseases because most chronic Diseases carry with them a great part of Job in neurodegenerative diseases such as Alzheimer’s disease (AD), Parkinson’s disease (PD), and Huntington’s disease (HD). Oxidative stress is accelerated by the ageing Process along with lack of dietary antioxidants. Almost in all studies it is founded that when we are intake large amount of dietary antioxidants reach this reduces the Alzheimer’s disease, it is Very imperative because treating a disease is harder than prevention of

disease preventing a disease. So Prevention is key and researches suggest that Preventing AD is actually not that complex. The treatment of Alzheimer’s disease with the use of antioxidants is hopefully because antioxidants slows down the progress of AD^[18].

Alpha-Lipoic acid^[19]

Alpha-lipoic acid (ALA) also plays an important role in functioning of brain, Alpha lipoic acid is an potent antioxidant it helps to increase metabolism of glucose and also increase the consumption in brain Alpha-lipoic acid can

improve cognitive performance and could be considered as a preventive treatment for

Alzheimer's disease.

Table 2: Nutraceuticals used in Alzheimer's diseases [23, 24]

DISEASE	NUTRACEUTICALS USED
Alzheimer's Disease	B-Carotene, curcumin, lutein, lycopene, turmeric etc may exert positive effects on specific diseases by neutralizing the negative effects of oxidative stress, mitochondrial dysfunction, and various forms of neural degeneration.

Cardiovascular disease

In all over world the diseases such as cardiovascular disease diabetes mellitus, obesity and cancers are increasing rapidly itsvery danger to human being. "Cardiovascular, word are combination of "cardio, means "heart, and "vascular, means blood vessels. Cardiovascular system is also known as circulatory system. Cardiovascular system refers tothat disease or disorderwhich isrelated to the blood vessels and heart, cardiovascular related diseases such as:- Hypertension (high blood pressure), Hypotension (low blood pressure), Coronaryheartdisease(heart attack) cerebrovasculardisease(stroke) , Heartfailure, Peripheralvasculardisease.

2001, chronic diseases contributed approximately 59% of the 56.5 million total Reported deaths in the world and 46% of the Global burden of disease. And in 1999 CVD Alone contributed to a third of global deaths and by 2010 it would be the leading cause of Death in developing countries. Majority of the CVD are preventable and controllable. It was Reported that low intake of fruits and Vegetables is associated with a high mortality In cardiovascular disease. Reported that low intake of fruits and Vegetables is associated with a high mortality In cardiovascular disease

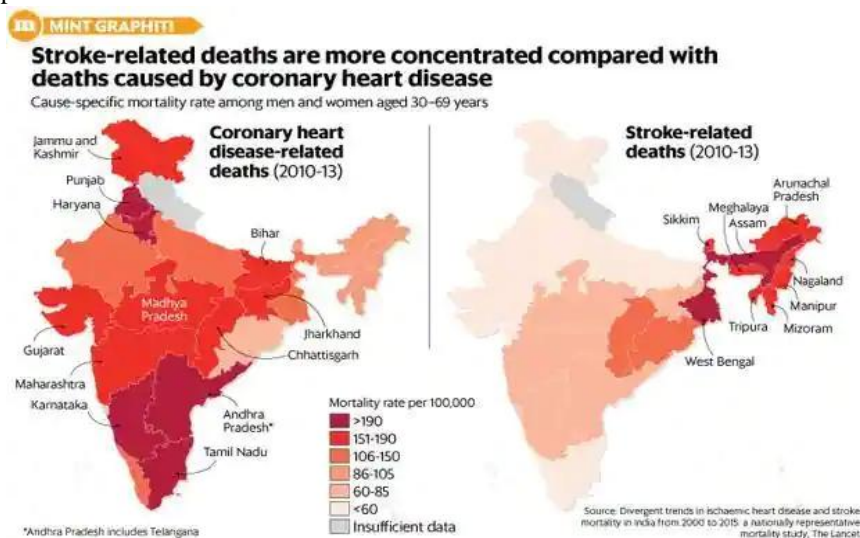


Figure 4. A study shows that heart ailments caused more than 2.1 Million deaths in India in 2015 at all ages. Graphic: Mint [22]

DISEASE	NUTRACEUTICALS USED
Cardiovascular Diseases	Anti-oxidants, Dietary fibers, Omega-3 poly unsaturated fatty acids, Vitamins, minerals for prevention and treatment of CVD. Polyphenols (in grape) prevent and control arterial diseases. Flavonoids (in onion, vegetables, grapes, red wine, apples, and cherries) block the ACE and strengthen the tiny capillaries that carry oxygen and essential nutrients to all cells. Milk and eggs having gamma linolenic acid (GLA) which has many benefits, including prevention and management of cardiovascular disease

Table 3: Nutraceuticals used in cardiovascular diseases [23-24, 25, 26]

In Apoptosis and Disease Prevention [27]

The different epidemiological animal model studies it is suggested that Nutraceuticals are largely herbal plant extract chemicals (phytochemicals) are from nutritional or medicinal plants. Some medicinal plants such as garlic, tea, ginger, and soybean containing the chemotherapeutic activity, by using these medicinal

plant we can prevent the further growth of cancer, Nutraceuticals in cultured human cells, specifically in apoptosis. In this section, we Review effects of some selected photochemical That belong with the following structural Classes: carotenoids, flavonoids, stilbenes, or Other sulphur-containing compounds

Table 4. Nutraceutical uses in apoptosis [27]

Phytochemicals	Source and content	Action
Carotenoids	Genistein, quercetin, Rutin Obtain from tomato Lycopene and β -carotene	Inhibit carcinogenesis in tumour cell Induce apoptosis in prostate cancer By DNA fragmentation, poly ADP-ribose polymerase (PARP) cleavage, and caspase-3 activation.
Stilbenes	Obtain from grapes, peanuts, and pines Resveratrol (3,5,4-trihydroxy-trans-stilbene)	Induces apoptosis and inhibits the growth of various human tumour cells, including oral squamous carcinoma, Promyelocytic leukaemia, human promyelocytic leukaemia, human breast cancer cells, and prostate and proteins

Osteoarthritis [28, 29]

Osteoarthritis (OA), an joint disease, it is most common type of arthritis in United States, it affected more than 21 million people's in United States in 2004, worldwide it affected millions of

people, it occurs when the protective cartilage that cushions the of the bones ends wears downs over time. Direct and indirect health care costs associated with all forms of arthritis were approximately 86 billion dollars.

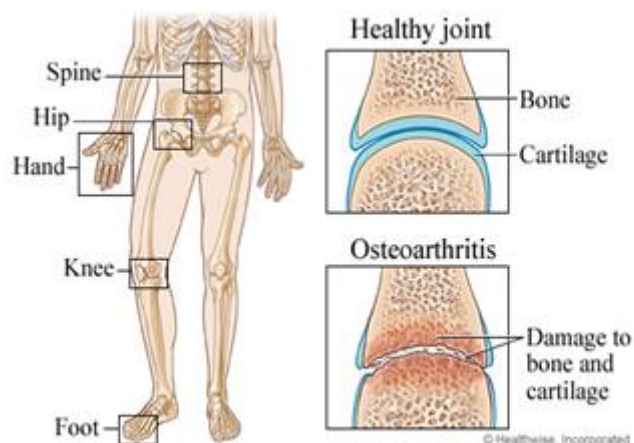


Figure 5. Joints after affected by Osteoarthritis

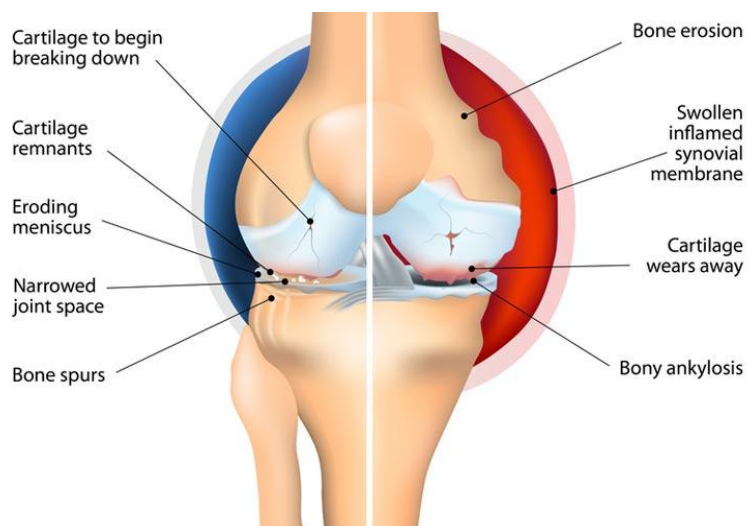


Figure 6. Joints affected from Rheumatoid arthritis

Rheumatoid arthritis [31]

When any patients are suffering from osteoarthritis disorder their physical activities are reduced because arthritis is very painful. Increased obesity possibly enhances the problem, through addition stress on joints. For the treatment and control the problems related to osteoarthritis these effective agents are uses glucosamine (GLA), and chondroitin sulphate (CS) by intake of these agents symptoms can be reduces. These nutraceuticals have both nutrients and pharmaceutical properties and also having anti-inflammatory property which reduces the inflammation and pain in (OA)^[28,29].

III. CONCLUSION:-

In this review we broadly discussed about nutraceuticals and their types. In this review we discuss about nutraceuticals pharmaceutical as well as nutritional properties. Nutraceuticals boosts the immune system of humans. In this review talk about how nutraceuticals affect the Diabetes mellitus how D.M is controlled by using these products. Other diseases which are discussed in this review are Alzheimer's diseases, cardiovascular disease, osteoarthritis, in apoptosis and disease prevention. In which nutraceuticals are effective for prevention and treatment of these diseases.

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