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Nutraceuticals as a Powerful Tool for Respiratory Diseases–An Overview

Abstract

The primary purpose of the lungs, a key component of the respiratory system, is to draw oxygen from the surrounding environment and make it available for aerobic respiration at the cellular level. The leading cause in today's world is reportedly respiratory, both acute and chronic. Respiratory conditions include bronchial asthma, chronic obstructive pulmonary diseases (COPD), pulmonary fibrosis, pneumonia, and lung cancer. In India, knowledge of herbal remedies was passed down through the generations. Currently nutraceuticals are getting substantial attention due to nutrition and therapeutic potentials. They have benefits over the medicine because they avoid side effects, On the basis of their source, they are categorized into different terms such as nutrients, dietary supplement' dietary fiber etc. Herbal nutraceutical is a powerful tool in maintaining health and acts against nutritional induced disease, thus promoting optimal health and quality of life. Studies have shown the promising results of nutraceuticals to treat several respiratory diseases. In the present review various ingredients which act as nutraceuticals (carbohydrates, lipids, edible flowers and medicinal plants) and application of nutraceuticals in respiratory disease has been discussed.

Keywords: Respiratory disease; Nutraceutical; Medicinal plant; Mineral and animal source

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Introduction

Hippocrates (460–377 BC), the father of modern medicine, almost 2500 years back established the relation of food and its importance for the treatment of various ailments in a very classical way optimizing various benefits. A nutraceuticals word is comprises of 'Nutrient' and 'Pharmaceuticals'. According to AAFCO, 1996, 'Nutrient' means a feed constituent in a form and at a level that will help, support a life of human being or animal while 'Nutraceutical' means any non-toxic food component that has scientifically proven health benefits including prevention and treatment of disease. Products isolated or purified from food are sold in medicinal forms not usually associated with food [1].

There is a vast cornucopia of herbs and foods which stimulate

support and nourish our body system. Some have been used by different traditional systems of several countries and are now being evaluated by modern research. Use of pharmaceutical antibiotic would build up tolerances which make it ineffective in the long run. It is a better way to choose such herbs in our daily life, which would be not only capable of normalizing our body functions (even in disease condition) but also preventive and nutritive, and they also boost our immune system. An herb may not act as precisely as an antibiotic but can act as antibacterial (even antiviral) by boosting our body's own defence mechanism. To feel as a healthy wellbeing, one of the prominent approaches is to stay away from stress and other lifestyle diseases. The following are some examples of herbs used as food as well as medicine during infection, to boost the immune system or even in several other illnesses [2].

Concept of Nutraceuticals

- A chemical that has physiological benefits or offers protection against chronic diseases is referred to as a nutraceutical.
- Enhance well-being
- Slow down ageing,
- Prevent chronic diseases
- Lengthen life expectancy
- Support the body's structure or functions

The heart keeps the lungs apart, and they each have a cone-shaped organ. The purpose of the respiratory system is to exchange carbon dioxide in the blood for oxygen. The respiratory system is responsible for controlling blood pH, olfactory receptors, sound production, and air filtering. Combining pharmaceuticals and nutraceuticals anything used both for nutritional and therapeutic purposes that is taken from herbs, nutrients, different diets, or processed meals. Most meal accessories contain nutraceuticals in varying concentrations [3].

Nutraceuticals are recognised as dietary supplements in the majority of countries. In order to verify the effects of prescription medications, it is essential to use medical check results from research and testing on animals. However, it used to be impossible to prove that specific compounds were useful at preventing disease. These products offer physiologic benefits in addition to providing protection against a number of diseases brought on by nutrient shortages. Mineral, animal, or plant sources can all be used to make nutraceuticals [4].

Many botanical ingredients found in many fruits, vegetables, cereals, fish, dairy, and meat products provide benefits beyond just providing food. That drug provides safety in opposition to persistent deficiency of the vitamins however additionally have physiology benefits. Nutraceuticals can be shape plant, animal and mineral source. Many fruits, veggies, grains, fish, diary and meat merchandise incorporate quite a few herbal elements that supply advantages past fundamental vitamin [5]. That substance has physiological benefits (or) provides safety in opposition to

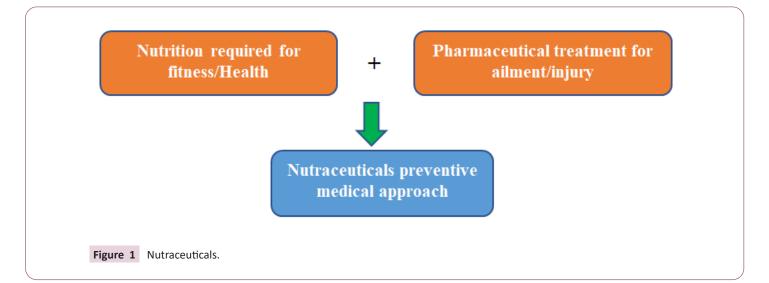
persistent diseases. However, in the previous there used to be no way to confirm the effectiveness of positive ingredients in stopping disease. This merchandise grant physiologic benefits in addition to offering defence in opposition to a range of illnesses added on with the aid of nutrient deficiencies [6].

Nutraceuticals can come from mineral, animal, or plant sources. Numerous foods like fruits, vegetables, cereals, fish, dairy, and meats include a variety of herbal components that have benefits beyond basic nutrition. That drug has physiological advantages or offers protection against chronic diseases. However, there was no method to verify in the past how beneficial certain compounds were at preventing sickness. These products provide physiologic benefits in addition to providing protection against a number of ailments that are made worse by nutrient shortages. Mineral, animal, or plant sources can all be used to make nutraceuticals. Many herbal ingredients that can be found in many fruits, vegetables, grains, seafood, dairy, and meat products have benefits that go beyond basic nutrition. This medication has beneficial physiological effects or offers protection against persistent illnesses [7].

Nutraceuticals can also be used to enhance health, prolong the getting old process, stop continual ailments, enlarge existence expectancy, or help the shape (or) function of the body. It is a prosperous supply of proteins, nutritional vitamins, minerals, dietary fibers, folic acid and carbohydrates, in most cases the resistant starches. It additionally incorporates distinct bioactive compounds such as lectins, enzyme inhibitors, phytates, oligosaccharides and phenolic compound [8] (Figure 1).

Application of Nutraceutical in Respiratory disease

Nutraceuticals products provide several pharmacological benefits like anti- aging, protection against some chronic disease, maintaining body homeostasis, cardiovascular diseases, neurodegenerative disease, and metabolic disorders like diabetes, degenerative disease, and metabolic disorders like diabetes, degenerative disease like cancer, protein deficiency, ophthalmic complications, allergic problems and Parkinsonism [9].



Lung disease

There's many numerous distinct forms of lung disorders, but the most well-known and deadly ones are bronchial sickness, lung cancer, chronic obstructive pulmonary disease, and lung infections such pneumonia or coronavirus (covid-19) infections. Numerous acute and enduring lung conditions are treated using a variety of herbal medications. Crude extract and other natural tools are essential. Lung disease is treated using the fruits, vegetables, and metabolites of many plants. As of December 2019, COV is the disease that is growing most quickly and causing the most financial and economic hardship in both developed and developing countries [10]. The number of articles about lung diseases has grown between 2016 and 2021.Because COV infections are the main cause of lung diseases, a cure is desired to stop infections and their horrifying progression. The treatments described for long illness contain bioactive substances (**Figure 2**).

The numerous plant varieties have a larger beneficial effect on the development and increased interest in lung diseases including COV and lung cancer due to the plant's spinoffs (covid-19) utilising gynogenic acid, resveratrol, baicalein, and haemachrome.

Curcumin and cisplatin, as well as calutron and gefitinib, are two examples of plant-based medications that have combined to provide a wonderful result. The plant off shoot delivers the greater effects and has consistently demonstrated to be the most effective treatment options. They could pave the way for additional drug development and the finding of life-threatening lung diseases like pneumonia, BA, and LC [11].

Bronchial asthma (Ba)

The use of patented products to treat physiological issues, focusing primarily on the interaction between several medications, for bio prospecting analysis and the discovery of new bioactive mixtures from common sources, has been extensively reported with ethnopharmacological attention [12]. These from specific attribute sources provide considerable contributions to the discovery of new therapeutic pharmaceuticals and their improvement, despite the enormous logical development regarding artificial and drug innovation on combining new tablets and atoms. Because they are practical and simple to use, drug agencies give corporations permission to conduct multiple studies that ex examine the therapeutic benefits, toxicity, and safety of many common things used in generic form [13] (Figure 3).

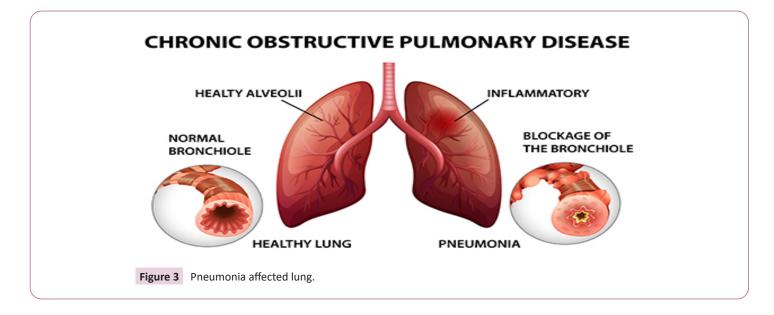
Around 40% of a common cure in the United States of America is addressed by the use of everyday goods, nutrients, and additional dietary modifications as assistant pharmaceuticals [14]. People with negative personality traits and fiery dispositions might wish to be exposed to the viruses that commonplace devices use. In fact, as the literature has revealed, the use of these items with biochemical structures involved in immunomodulation should be added to the management of these diseases. Since more than 5000 years ago, products based on flora have been used as a common therapy for BA [15]. Their use is linked to Chinese lifestyles that were developed as a result of the imbuement of Ephedra silica as a safe form that started off organised to decrease BA crises the study focused on beet, honey, garlic, yarrow, onion, lemon, and mint, showcasing the range of characteristic objects used in children's BA treatment. Additionally, other commonly deduced substances have also been widely mentioned in the BA treatment, such as common oils derived from plants and animals that can be concentrated to a smaller volume [16]. Frequent oils derived from plants attempt to cure BA reciprocally. The main everyday items are used because of mixtures, such as the most bioactive mixtures of mono and sesquiterpenes and phenylpropanoids, which have sedative, antifungal, alleviating, and antibacterial properties. Immediately increase the level of endogenous adrenal cortical steroid, including when combined with NF-B NF-kB pathway's guiding principle, which includes lowering bodily fluid entry and aggravation in lung tissues [17].

Cytokine herbal Immunomodulator for Bronchial asthma

Their biosynthetic origin demonstrates that numerous herbs and spices from common combinations can also effectively beautify BA anticipation or treatment [18]. Asthma-related bioactive mixtures can also be divided into five categories based on their real-world structures and biological effects: flavonoids, alkaloids, polyphenols, glycosides, and terpenoids. Triterpenoids, glycosides, flavonoids, alkaloids, and polyphenols are five fundamental groups that have been examined,



Figure 2 Normal lung. Affected lung.



coupled with specific combinations, specifically triptolide, that have demonstrated extraordinary action supportive of flamboyant cytokine articulation in BA patients [19]. These mixes' target pathways are only hazy. Whatever the case, a few immunomodulatory factors are described. Flavonoids are superb cancer prevention agents that suppress unusual structures like basophils and pole cells as well as artificial intermediary starting Th2-type cytokine combination. The aryl hydrocarbon receptor was activated by flavonoid, which inhibits IL-4-induced signal transduction and impacts the separation of T cells [20]. The NFkB goal route is the one that polyphenols have an impact on. Polyphenols suppress T partner 2 initiations and promote the development of administrative T cells (Tr). Flavonoids can also stabilise DC functions by inhibiting MHC-II and, consequently, the costimulatory particle articulation or by limiting cytokine production, thereby impeding the antigen introduction process. Triterpene glycosides also influence the NF-kB flagging pathway and act as mitigating agents. Alkaloids' effects on STAT6, field P3 (Foxp3), NF-kB, and MAPK signalling pathways to control highly potent cytokine induction [21].

Chronic obstructive pulmonary disease

One of the leading causes of mortality and morbidity worldwide is COPD. Smoking is the most important risk factor among many others. However, smoking by itself is no longer sufficient to explain all the symptoms of COPD. Even non-smokers can get COPD, especially in areas of the world where biomass exposure is prevalent [22]. More than half of smokers do not currently have worsening COPD. Despite quitting smoking, a fraction of COPD patients exhibits chronic discomfort. Furthermore, acute COPD exacerbations and rapid lung feature loss might occur without regard to smoking. To control the disease, it is crucial to clarify additional contributing factors that are not related to smoking [23]. The tiny airways' persistent infection is one of COPD's defining features. One important factor in the development and acute worsening of the condition is respiratory tract pollution. In the majority of immune-competent and asymptomatic COPD patients, antiviral treatment is no longer necessary. Antiviral

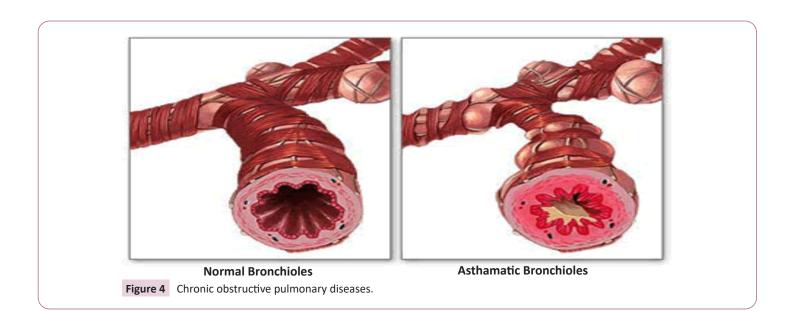
treatment is no longer entirely recommended due to a confirmed COPD outcome. Nowadays, pharmaceutical administration is not required because the majority of endemic viral infections are self-limiting. Oseltamivir is recommended when the medical prognosis for a severe and novel pandemic influenza virus is determined [24]. Not prescribing antibiotics when they are no longer required is now one of the difficult decisions. Antibiotics are often not essential when a virus is the primary organism unless one is concerned about submitting viral secondary bacterial lung infections. Although sputum characteristics no longer identify the causing organisms, sputum purulence can still be used to guide antibiotic usage. Surprisingly, influenza immunisation is advised for COPD and other chronic lung illnesses patients [25] (**Figure 4**).

Allergic disorder

Due to the human immune system's sensitivity, allergies are a prevalent condition. The majority of allergy reasons are either unknown or difficult to identify, making clinical therapy complicated. The body changes a range of allergic reactions, from minor irritability to potentially catastrophic ones like severe respiratory distress [26]. Haematological alterations include an increase in white blood cell and basophil count is related to allergic conditions. Because of its effects on low density lipoprotein, the plant bioactive quercetin is frequently employed in nutraceuticals for the control of allergies. Another plant derivative primarily applied in nutraceuticals for allergy control is eucalyptus essential oil [27].

Natural Nutraceuticals products from animals

Fish oil: The omega-3 fatty acids docosahexaenoic acid (DHA) and eicosatetraenoic acid are found in fish oil, which is a good source of these nutrients (EPA). In patients with age-related respiratory disorders, omega-3 is a commonly used anti-inflammatory vitamin. Researchers believe that DHA and EPA are the two most significant components of fish oil [28]. Numerous studies have suggested that high-energy foods play a role in chronic diseases including COPD and pulmonary fibrosis as well as infections. DHA might also help to prevent lung fibrosis brought on by bleomycin.



Diets that are high in EPA and DHA are the best nutritional choices for managing various types of lung problem progressions [29].

Heparin: According to the WHO Model List of Essential Medicines, heparin-based remedy is a secure and tremendous remedy strategy. Heparin is recognized for its capability of altering the clotting responses in the human circulatory machine [30]. Heparin has acquired interest due to its shocking function in anticoagulant feature and it's doable in inhibiting procollagen fiber crosslinking. Therefore, it is regarded to be a conceivable therapeutic choice for fibrotic ailments. Heparin has been accepted by means of each FDA and WHO and has been commercialized as a drug and dietary supplement; furthermore, it has been broadly used to treat bronchial asthma and idiopathic pulmonary fibrosis [31]. It has been stated that heparin ought to assist sufferers with IPF to minimize soreness or alleviate aggravated responses. The mechanism underlying the motion of heparin includes stopping the cross-linking of procollagen fibers via inhibiting lysyl oxidase. In the absence of the cross-linking of procollagen fibers, overscarring and fibrotic development should now not continue [32].

Surfactants: In preterm new-borns with respiratory distress syndrome, surfactant replacement therapy lowers mortality and morbidity (RDS). Surfactants come in two varieties: synthetic protein-free zones and those originating from animals. Despite the fact that both forms of surfactants are efficient in the treatment and prevention of RDS, meta-analyses have shown that using animal-derived surfactants leads to earlier improvements in ventilator support, better mortality rates, and lower rates of pneumothoraxes [33]. The content of phospholipids, surfactant proteins B and C, plasmalogens, viscosity, and volume administration vary amongst animal-derived surfactants. RDS in premature new-borns is frequently treated with bovine lipid extract surfactant. It is a natural bovine pulmonary surfactant extract with a phospholipid content of 27 mg/mL and 1% SP-B and SP-C. Despite being widely used, BLES has only a small number of published trials for the treatment of RDS in preterm newborns. The advantages of artificial or animal-derived surfactants for treating or preventing respiratory distress syndrome,

Administration of surfactants decreases distress syndrome, and as a result, ventilation and prolonged oxygen therapy [34]. Infants at risk for respiratory distress syndrome are demonstrated to have a better clinical result when given surfactant formulations. Animal-derived surfactant formulations have been shown to lower mortality and pneumothorax risk in clinical trials. The four native surfactant proteins SP-A, B, C, and D have been identified. Native pulmonary surfactant protein concentrations in animalderived products may vary from batch to batch. Concern has also been raised about animal-source infections. When respiratory distress syndrome is in its acute phase and infant mortality is being reduced, animal-derived surfactants appear to be superior to synthetic surfactants [35] (**Figure 5**).

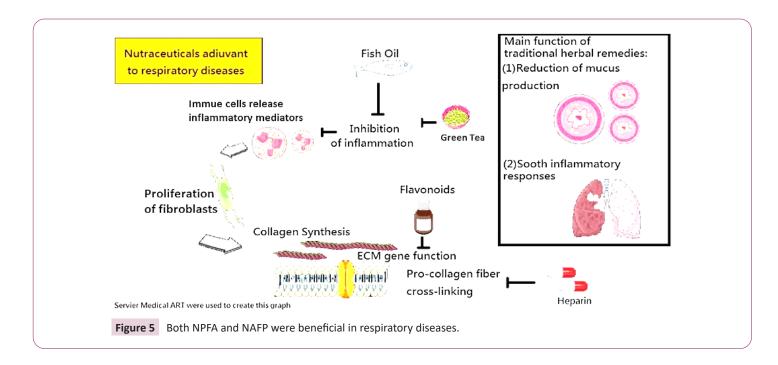
Natural Products from Plants (NPFP): Plant-derived natural products (NPFP) have been shown to have an impact on respiratory disorders. The natural substance is having an impact on respiratory-related issues, and the immune system of the body is involved. There are numerous natural products with therapeutic benefits for treating acute lung injury and acute respiratory illnesses syndrome. They include terpenoids, alkaloids, flavonoids, glycosides, and others that are used to treat respiratory-related issues [36].

Alkaloids: Curcumin, an alkaloid substance, reduces allergic airway inflammation and hyper reactivity by preventing the NF-KB signalling pathway from being activated. By activating the NF-KB signalling system, curcumin longa linn rhizome curcumin, which contains alkaloid, is utilised to reduce allergic airway inflammation. Curcumin protects once more in LPS-activated raw 2647 cells by preserving 1KB and suppressing p50 and p65 nuclear translocation [37].

Quercetin: Quercetin (3, 31, 41, 5, 7-pentahydroxy flavone) is a naturally occurring polyherbal flavonoid that is obtained from camellia sinuses. It is used to treat lipid peroxidation, inflammation, oxidative stress, increased capillary permeability and platelet aggregation inhibition [38].

Lycopene: A powerful anti-oxidant chemical called lycopene is





obtained from the solanum co Persico plant. Through a redox process, lycopene inhibits NF-KB and shields cells against asthmatic inflammation [39].

Oxygen interacts with lipids, protein, and nucleic acids each hastily and conveniently. The ROS device requires enough oxidation-reducing elements such as steel vitamin and diet consumption. Under positive quantities of the precursors of TGF, the wide variety of macrophages will expand drastically. NPFPs have been pronounced to forestall persistent inflammatory responses, thereby without difficulty activating the innate immune responses [40].

Green tea: Consumption of inexperienced tea has been validated to be really useful to sufferers with kind two diabetes and lung most cancers in addition, inexperienced tea possesses robust antioxidant and anti-inflammatory effects. Epigallocatechin gallate (EGCG) has been regarded to be the most necessary dietary aspect of inexperienced tea taking part in a position in pulmonary fibrosis [41]. EGCG has giant manageable in inhibiting chemo attractants and regulating inflammatory responses in more than one fibrotic disease. In addition, in vivo research has demonstrated that EGCG is advisable in ameliorating the lung accidents of rats uncovered to cigarette smoke [42]. Therefore, EGCG has an excessive viable in enhancing the well-being of sufferers with respiratory diseases. The human liver can assist in metabolizing EGCG into theaflavins. Theaflavin is an herbal phenol extracted from black tea; it is shaped via the fermentation of inexperienced tea. Several NPFPs exert their anti-inflammatory results by means of interfering with infection associated pathways and activator protein 1(AP1) and the nuclear factor (NF)-kB pathway by ingesting inexperienced tea, sufferers can concurrently acquire the dietary advantages of each EGCG and theaflavins [43].

Flavonoids: Flavonoids are recognised for their functionality of

decreasing the expression of ECM genes. In general, flavonoids work as managers in the human physique. It has been mentioned that quercetin is a key modulating flavonoid [44]. Quercetin can disturb the redox stability in pulmonary fibrosis. The key component of this modulation is Nrf2. Quercetin can assist enlarge the Nrf2 activity, as a result elevating the antioxidant response as a consequence [45]. Therefore, growing the consumption of greens and fruits no longer solely will increase the consumption of flavonoids. However additionally decrease the manufacturing of proinflammatory cytokines such as IL-8 and TNF-tenuously? From in vivo experiments to cutting-edge FDAapproved dietary helps, NPFAs are cruciate dietary pattern [46]. Nutrients are bendy supplements, now not constant therapeutic packages, and they can be mixed with distinct dietary patterns, cooking styles, and cultural backgrounds. Therefore, even though all the NPFAs and NPFPs are recommended to respiratory health, combining them accurately might also be the first-rate suit for affected person care. By interfering actively with dietary patterns, they would possibly steadily enhance the patient's fitness prerequisites and survival [47]. However, concerning NPFAs such as heparin, they would possibly in reality inhibit the development of ailments and extend the patient's prognosis except the want for synthetic tablets or interventions. Respiratory illnesses are exceedingly associated to irritation. Therefore, ameliorating the dysregulated inflammatory responses in the lung can without delay soothe the patient's circumstance. By reducing the ROS ranges actively, focusing on antioxidant degrees, and blocking off the inflammatory response-related signalling pathways, dietary sample administration can assist in stopping the sickness development [48]. DHA, EPA, and heparin are all famous NPFAs that are advisable in the administration of ailment progression. For instance, fish oil offers with the inflammatory signalling pathways, whilst heparin disrupts the fibrotic development via procollagen [49].

Natural nutraceuticals products from minerals

It has also been discovered that several minerals are protective in respiratory disorders. Increased consumption of magnesium, calcium, and potassium in children is negatively correlated with asthma prevalence [50]. Despite the inconsistent outcomes of numerous observational and experimental studies, a randomised, a low-sodium diet provided no therapeutic advantage for bronchial reactivity in persons with asthma, according to a controlled trial [51]. In people with asthma, dietary magnesium may have positive bronchodilator effects. Low dietary magnesium intake has been linked to both decreased lung function in kids and adverse effects on bronchial smooth muscle in people with severe asthma [52]. Before its significance in asthma and recommendations can be established, more proof of beneficial therapeutic benefits is needed. Asthmatics have been demonstrated to have lower dietary selenium intake than non-asthmatics [53] and maternal plasma selenium levels have been reported to be negatively correlated with asthma symptoms. Case control studies on children, however, have not discovered a connection between selenium intake or levels and outcomes related to asthma [54]. Additionally, findings from a sizable, carefully planned RCT in individuals with asthma revealed no beneficial effects of selenium supplementation [55]. Selenium levels in cord blood were negatively correlated with chronic wheezing, while iron levels were negatively correlated with lateronset wheezing in children [56], indicating the significance of appropriate dietary consumption throughout pregnancy. Mineral intake and COPD connections are scarce. In older participants with severe COPD, folic acid and selenium intakes were found to be below recommended levels. Serum calcium levels were also found to be low, despite appropriate calcium intake, which was probably caused by low vitamin D status. However, there is little support for supplementing [57]. Mineral intake may be significant in respiratory illnesses. It's possible that getting enough of these nutrients through a balanced diet is sufficient.

Nutraceuticals in drug delivery

As nutraceuticals are mostly absorbed by oral route the major concern is that the absorption of nutraceuticals product by the gastrointestinal tract and also its fate after fast pass metabolism. This presents a unique challenge to many nutraceuticals products and so research thrust in their delivery approaches is now gaining momentum [58]. For example milk thistle plant extracts recommended for hepatoprotection [59]. The main bioactive components of the extract silymarin suffer from degradation in the GIT which is a major setback to the efficacy of the nutraceuticals. Similar problems are also observed in different bio actives like alpha -tocopherol, ascorbic acid, curcumin, green tea extract, lycopene used in various nutraceuticals formulations. The most promising and widely explored approach in nutraceutical drug delivery is based on nanotechnological interventions [60]. Nanoscale delivery of nutraceuticals has a definite impact on the absorption and distribution kinetics of the nutraceuticals leadings to products efficacy enhancements. They not only enhance their absorption and bioavailability but also provide protection to the nutraceuticals against GIT degradation and first pass effect. Besides these nano-devices provides provide site-directed delivery of nutraceuticals which significantly reduce chances of residual toxicity. Liquid encapsulation technology in nutraceutical formulation allows pellets, oils granules and powders to be incorporated in hard gelatin capsule. But in spite of several advantages of such products their on the cost of nutraceuticals would actually play a vital role in consumer acceptance and their future [61].

The future of nutraceuticals

In global market presently a large number of nutraceuticals formulations are available with diverse bio actives ranging from vitamins to plant bio actives. The high consumer acceptance can be traced to low health risks compared to synthetic drugs. Customers are showing keen interest in different types of nutraceuticals for relieving stress, boosting energies, mental alertness, preventative metabolic disorders, combating oxidation stress etc. [62].

Conclusion

It concluded that, nutraceuticals area potentially growing sector and are engaged in both the fields, either medical treatment or nutrition so as to assure integrated medical assistance. These act as potential dietary supplements, prevention of diseases such as COPD, the support and treatment of various types of cancer, and other healthcare benefits. Natural products have been known for their therapeutic values for centuries. In the modern era, these substances have been used as an immunity booster; antidiabetic, anticancer, antimicrobial, and gastro protective agents; and so on. Therefore, these herbs could be better options to be formulated as nutraceuticals. Hence, nutraceutical industries now understand and perceive extensively about the potential success of nutrients that affect people in healthcare. The scientific research ratifies that the improved safety and potential effects of newly developed nutraceutical products will further stimulate the investments in newer technologies, such as nutrigenomics, converging techniques, varied imaging technologies and its applications in nutrition development and healthcare. People have to change their mind set and adopt a new style of healthy living and taking food to make a new concept "Health for All".

Conflict of Interest

The authors declare that they have no conflicts of interest.

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