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Role of medicinal plants on inflammatory diseases: A review

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Abstract

Medicinal plants are widely used to promote good health and treat diseases. However due to lack of standardized formulations and systematic studies such as pharmacological target and mechanism of action, it has not been developed as mainstream pharmacotherapy. Over a decade of studies provide a compelling evidence for targeting Nrf2 for treatment of oxidative stress-driven chronic disease including COPD, asthma, rhinosinusitis, cardiovascular disease, diabetes, Parkinson's disease and Alzheimer disease. Transcription factor Nrf2 is master regulator of an adaptive cytoprotective stress response program, which includes nearly all cellular antioxidant genes involving in inhibition of oxidative stress. Pharmacological activators of Nrf2 are shown to protect from or mitigate progression of various chronic diseases. Diverse classes of phytochemical such as polyphenol, triterpenoid, isothiocyanate or flavonoid are shown to be potent activators of Nrf2 pathway.

Keywords: Nrf2, Indian tradition and oxidative stress

Introduction

“Let food be the medicine and medicine be the food.” According to the worldwide weight of sickness study, the non-transmittable infections (NCD, for example, ischemic coronary illness, cerebrovascular infection, COPD, diabetes, neurological disorders and cancer are major cause of death and disability in India and globally. Risks for NCD are attributed to exposures to environmental stressors such as tobacco smoke, air pollution, high calorie diet and carcinogens. Although, in the past two decades, life expectancy has increased to around 70 yr, the quality of life is greatly reduced due to NCD in India. There is urgent need for new therapies to halt or mitigate the disease progression and improve the quality of life^[1,2]. Chronic inflammation promotes the tissue damage and ultimately leading to organ injury and onset of disease symptoms. However, chronic intake of drugs is associated with severe side effects. More importantly, drugs are ineffective in blocking the underlying mechanistic cause of the disease. Therefore, there is need for therapeutic agents which not only mitigate inflammation, but also inhibit oxidative stress and improve tissue repair. This demonstrates the feasibility of developing plant extracts targeting Nrf2 as dietary supplements or nutraceuticals for improving health in high-risk population. Unfortunately, there are no systematic studies undertaken to screen the Ayurvedic medical plants for Nrf2 activity.

Disease prevention

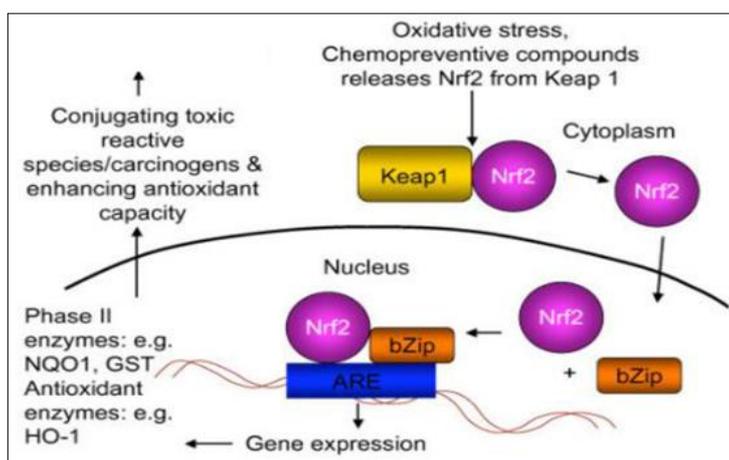


Fig 1: Role of Nrf2 in oxidative stress

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Review of literature

Ayurvedic medicines

From ancient times, Ayurvedic medicine is being widely used as dietary supplements or therapeutics to prevent or treat number of inflammatory diseases. However even today, ayurvedic medicine has not been integrated with the mainstream clinical practice. The major obstacle lack of underlying biological mechanisms of action of plant extracts. Other factors include lack of documented validation of products and quality assurance and toxicity profile. Due to side effects, over use and poor efficacy of mainstream medicines to halt or cure NCD, many people are choosing plant based medicine to prevent or treatment of diseases. There is urgent need for robust systematic mechanistic basic and translation research to bring the plant medicine into mainstream medicine [3].

Medicinal properties of plant extracts is attributed to bioactive metabolites belonging to diverse chemical classes such as triterpenoid, polyphenols, flavonoids, isothiocyanates etc. Based on the composition and levels bioactive compounds, plants exhibit different biological activity [4]. Therefore, the systematic evaluation of traditionally used herbal medicine by employing state of art technologies and target based bioassay is highly relevant and scientifically challenging line of investigation.

As of late there has been a move in general pattern from manufactured to home grown medication, which we can say 'Re-visitation of Natures' Restorative plants have been known for centuries and are profoundly regarded everywhere on the world as a rich wellspring of restorative specialists for the avoidance of infections and diseases. Nature has offered our country with a gigantic abundance of therapeutic plants; in this way India has frequently been alluded to as the Medicinal Garden of the world. Nations with antiquated developments, for example, China, India, South America, Egypt, and so on are as yet utilizing a few plant solutions for different conditions. In such manner India has a one of a kind situation in the world, where various perceived native frameworks of medication viz., Ayurveda, Siddha, Unani, Homeopathy, Yoga and Naturopathy are being utilized for the health care of people. No doubts that the herbal drugs are popular among rural and urban community of India.

The one explanation behind the prevalence and worthiness is conviction that all regular items are protected. The interest for plant based medications, wellbeing items, drugs, food supplement, makeup and so forth are expanding in both creating and created nations, because of the developing acknowledgment that the normal items are non-poisonous, have less results and effectively accessible at reasonable costs [5]. Presently a days, there is a restoration of interest with natural based medication because of the expanding acknowledgment of the wellbeing dangers related with the unpredictable utilization of present day medication and the natural medication businesses is currently exceptionally quickly developing area in the global market. Be that as it

may, shockingly, India has not done well in this worldwide exchange of natural industry because of absence of logical contribution to home grown medications. In this way, it is suitable to feature the market capability of home grown items and that would open conduit for improvement of market potential in India [6]. With these items, we assessed here the market capability of home grown medication in India. Anti-inflammatory effects of Nrf2 Controlling inflammation is critical for preventing various diseases such as infectious disease, allergies, COPD, autoimmune diseases, cancer and metabolic syndrome. Evidence suggests that Nrf2 is essential for controlling redox regulation of TLR signalling via NADPH oxidase activity. Compared with wild-type, in response lipopolysaccharide (LPS, a bacterial component) stimulus, Nrf2 knockout macrophages showed enhanced ROS production via [7].

NADPH oxidase activity, greater activation of TLR4 and subsequent downstream recruitment of MyD88 and Toll/IL-1R (TRIF) domain-containing adaptor leading to greater activation of NF-KB and IRF3 signalling [8].

Phytochemicals as activators of Nrf2 pathway

Over the past few decades, there has been a growing body of interest in identifying naturally occurring cytoprotective agents, particularly those present in our diet. Plants, plant extracts, and compounds purified from plants are used in traditional medicine including Ayurveda for prevention, mitigation and cure of diseases. However, due to lack of knowledge related to pharmacological and toxicological mechanisms, these natural products are not in use as main stay therapy [9].

A wide variety of dietary phytochemicals have been reported to induce the expression of enzymes involved in both cellular antioxidant defenses and inactivation of electrophilic toxicant. Several phytochemical belonging to polyphenols, curcumin, quercetin, flavonoids, isothiocyanate (sulforaphane), and triterpenoids have shown to be very effective in activating Nrf2 pathway [10]. Among these phytochemicals, Sulforaphane, an edible isothiocyanate, has been extensively studied for health benefits in both normal and high-risk human subjects (Asthma, diabetes, COPD, cancer, hypertension, autism) [11, 12] (table 1). This demonstrates feasibility of developing plant extracts targeting Nrf2 as dietary supplements for improving health in high-risk population. Unfortunately, there are no systemic studies undertaken to screen the Ayurvedic medicinal plants for Nrf2 activity.

In contrast, over 70% of all the drugs approved till date are either derived from or structurally similar to natural compounds indicating the necessity of screening natural product. There is a great demand for screening natural products against a specific pharmacological target for discovery and development of natural products as dietary supplement or nutraceuticals or purified compound [13].

Table 1: Nrf2 protects from several inflammatory diseases market value of Nrf2 targeted therapeutics [14]

Neurodegenerative disease	Diabetic co-morbidities
▪ Alzheimer's disease	▪ Retinopathy
▪ Parkinson's disease	▪ Nephropathy
▪ Stroke	Macular degeneration
Respiratory disease	Acetaminophen drug toxicity
▪ COPD	Alcohol toxicity
▪ Asthma	Skin disorders
▪ Acute lung injury	▪ Epidermolysis bullosa simplex

▪ Pulmonary fibrosis	▪ UV induced skin injury
Infectious disease	Autoimmune disease (IBD)
▪ Sepsis ▪ Bacterial/viral inflammation	▪ Lupus

Table 2: Clinical studies sulforaphane broccoli sprout extract

Title	Conditions
Sulforaphane in Treating Patients With Recurrent Prostate Cancer	Prostate Cancer
Impacts of Sulforaphane (SFN) on Immune Response, A 6-month Study to Evaluate Sulforaphane add - on Effects in	Schizophrenia
A 12-weeks Study to Evaluate Sulforaphane in Treatment of Autism Spectrum Disorder	Autism Spectrum Disorder
Broccoli Sprout Extracts Trial	COPD
Sulforaphane-rich Broccoli Sprout Extract for Autism	Autism
Sulforaphane Supplementation in Atopic Asthmatics	Asthma
Effect of Sulforaphane in Broccoli Sprouts on Nrf2 Activation	Cystic Fibrosis
Topical Application of Sulforaphane containing Broccoli Sprout Extracts on Radiation Dermatitis	Breast Cancer Dermatitis
Clinical Trial With Broccoli Sprout Extract to Patients With Type 2 Diabetes	Diabetes Mellitus, Non-Insulin Dependent
Effects of Sulforaphane (SFN) on Immune Response to Live Attenuated Influenza Virus in Smokers and Nonsmokers	Smoking
Impact of Sulforaphane - rich Broccoli Sprout Homogenate on Ozone Induced Inflammation Through Modulation of NRF2	Healthy
Broccoli Sprout Intervention in Qidong, P.R. China	Environmental Carcinogenesis
Broccoli Sprout Extracts in Healthy Volunteers: A Pilot Study of Nrf2 Pathway Modulation in Oral Mucosa	Healthy Subject

Objectives

Use of medicinal plants in revolving Indian traditional methods to inhibit diseases and its effect on ameliorate Indian economy.

Hypothesis

Hypothesize that medicinal plants are potential source of phytochemical activators to prevent or mitigate the progression of inflammatory diseases by diminishing oxidative stress and inflammation caused by exposures to environmental toxins.

Discussion

Nutrition is a fundamental need. Different risk factors identified with wellbeing result from lopsidedness in nourishment. These awkward natures in India are generally common prompting unfavorable results. A certain section of the population consumes diet which does not provide sufficient calories, let alone sufficient nutrients. In India, nearly 20% of the total population and 44% of young children (below 5 years of age) are undernourished and underweight [15].

On the other hand, there is a huge population that is nourished in calorie intake but not in terms of nutrient intake. This segment would typically include lower middle to upper class population with sufficient purchasing capacity but probably less awareness about their nutrient requirements, leading to imbalanced nutritional uptake. In fact, in our population about 30% in urban and 34% in rural areas consume more than the recommended number of calories with higher than recommended levels of dietary fats and could be the biggest supporter in making India the future cardiovascular and diabetes capital of the world. The third population segment, which is about 80 million, consumes nutrients and calories more than those recommended for the lifestyle they have opted for. The principle hazard factors in agricultural nations like India are identified with sustenance and add to almost 40% of all out death and 39% of total disease burden. The main leading risk factors in developing countries [16]. As per WHO report, India has high magnitude of cardiovascular

infections and biggest number of diabetes patients on the world. The number of cardiovascular diseases patients in Brazil, Russia, China, and India are 4.1, 11.8, 24.5, and 28.9million, respectively. Moreover the quantities of diabetes patients in same nations are 4.6, 4.6, 20.8, and 31.7 million, individually. An estimate of the cost of productivity lost on account of mortality due to nutrition related disorders was estimated to be 0.85% of the GDP in 2004 and is expected to increase up to 1.2% for India's GDP by 2015. Nearly 340 million people, 30% of the population in urban areas and 34% of the population in rural areas, consume calories more than the norms. Hence, the requirement of external intervention, that can supplement diet to help prevent nutrition-related disorders and promote wellness over treatment of various diseases, has become a necessity, and such products are known as nutraceuticals. A nutraceutical is a food or food segment that professes to have medical advantages, including therapy and avoidance of illness. Nutraceuticals, an arising idea, can be extensively arranged as items which are separated from characteristic sources (nature-like) or fabricated artificially (man-made), which supplement the eating routine to give sustenance far beyond ordinary food and help forestall nourishment related issues. The nutraceutical industry is rapidly growing (7%-12% per year). With broad narrative information on energizing wellbeing results, nutraceuticals guarantee critical commitments to illness counteraction. The worldwide nutraceutical market is assessed at 117 billion US dollar of which India's share is as small 0.9%.

United States and Japan are key markets for nutraceutical consumption. Indian nutraceuticals market is about 1 billion USD which is increasing day by day. Globally, this market is expected to reach 177 billion USD in 2013. The dietary supplements category is expected to be the fastest growing product category globally. To identify the best plant extract which is amenable for further development as nutraceuticals or dietary supplement. To the least, pilot study has to establish the standardized extraction protocols and NQO1 activity screening platform for identifying Nrf2 inducers.

Conclusion

India is setting on a well-recorded and well-practiced knowledge of traditional herbal medicine. The basic requirements for gaining entry into developed countries include well-documented traditional use, Single-plant medicines, Medicinal plants free from pesticides, heavy metals etc., Standardization based on chemical and activity profile and safety and stability. Herbal drug development is possible only through the development of standardized herbal products. The health care systems are going to become more and more expensive therefore, we have to develop technologies to essentially introduce and integrate herbal medicine system in our health care. There is a gigantic extension for India additionally to arise as a significant part in the worldwide home grown item based medication which allows us to trust that medication fabricated as per standards of Ayurveda, Siddha and Unani will arrive at new skylines and makes them the best on the planet if the nature of the home grown medications is monitored after, adequacy would it self be kept up and there will be nothing to prevent them from rivaling the advanced medication with added points of interest fewer side effects and of lower costs.

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