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NUTRACEUTICALS AN EMERGING CONCEPT ON NONI FRUITS: A BRIEF REVIEW

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Abstract

Products derived from Noni fruit (Morinda Citrifolia) have been commercialised in the USA since the 1990s and are increasingly distributed all over the world. A large number of beneficial effects have been claimed for Noni. Fruit juice of Noni has been approved as a Novel Food by the European Commission in 2003. This article reviews current knowledge on the phytochemistry, pharmacology, safety aspects of Noni fruit and Noni-derived products, and health-related claims and benefits. The knowledge on the chemical composition of noni fruit has considerably increased over recent years. A number of in vitro and, to a certain extent, in vivo studies demonstrate a range of potentially beneficial effects. However, clinical data are essentially lacking. To what extent the findings from experimental pharmacological studies are of potential clinical relevance is not clear at present. Based on a toxicological assessment, noni juice was considered as safe. Due to recent reports of cases of hepatotoxicity, the safety issue has been re-examined in Europe. While the European Food Safety Authority sees no link between adverse effects on liver and consumption of noni juice, a continuing monitoring of the situation is desirable and some vigilance advised.

Keywords

Noni, Morinda citrifolia, Rubiaceae, Novel food, Phytochemistry, Pharmacology, Hepatotoxicity.

Introduction

Nutraceuticals is a term derived from "nutrition" and "pharmaceutics." The term is applied to products that are isolated from herbal products, dietary supplements (nutrients), specific diets, and processed foods such as cereals, soups, and beverages that other than nutrition are also used as medicine. Nutraceuticals are products, which other than nutrition are also used as medicine. A nutraceuticals product may be defined as a substance, which has physiological benefits or provides protection against chronic disease. Nutraceuticals may be used to improve health, delay the aging process, prevent chronic diseases, increases life expectancy, or support the structure or function of the body. Nowadays, nutraceuticals have received considerable interest due to potential nutritional, safety and therapeutic effects. Recent studied have shown promising results for these compounds in various complications. In the present review much effort has been devoted to present new concepts about nutraceuticals based on their diseases modifying indications. Emphasis has been made to present herbal nutraceuticals effective on hard curative disorders related to oxidative stress including allergy,

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Alzheimer, cardiovascular, cancer, diabetes, eye, immune, inflammatory and Parkinson's diseases as well as obesity. The recently published papers about different aspects of nutraceuticals as alternative for pharmaceuticals were searched using scientific sites such as Medline, PubMed, and Google Scholar. [1,2] In the US, the term 'nutraceutical' products are regulated as drugs, food ingredients and dietary supplements. Nutraceuticals, in contrast to pharmaceuticals, are substances, which usually have not patent protection. Both pharmaceutical and nutraceuticals compounds might be used to cure or prevent diseases, but only pharmaceutical compounds have governmental sanction. A dietary supplement is considered as a product that bears or contains one or more of the following dietary ingredients: A mineral, a vitamin, an amino acid, a medical herb or other botanical, a dietary substance for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients. Nutraceuticals are of these nutritional supplements which are used for health purposes other than nutrition. Some popular nutraceuticals include ginseng, Echinacea, green tea, glucosamine, omega-3, lutein, folic acid, and cod liver oil. Majority of the nutraceuticals possess multiple therapeutic properties. [3,4]

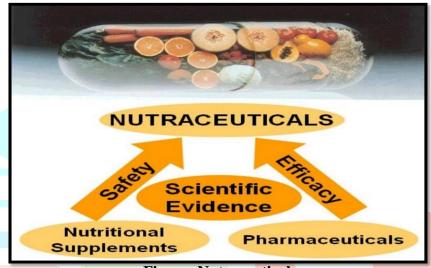


Figure: Nutraceuticals

Advantages of Nutraceuticals [5]

- Improve health.
- Delay aging.
- Easily available and cheap.
- ➤ Increases life expectancy.
- > Reduced side effects with desirable outcomes.
- ➤ Holistic approach.
- > Provide dietary supplement naturally.
- It provides food for populations with special needs (eg: nutrient-dense food for the elderly).

Disadvantages of Nutraceuticals [6]

- They are not subjected to testing and regulations same as pharmaceuticals.
- They are not regulated by authority boards like FDA.
- > The bioavailability of nutraceuticals is low.
- Unregulated products are created with only meeting the profit margins.
- No regulatory definition.

Morinda Citrifolia (Noni) Fruit

Products derived from the fruit of Morinda citrifolia (Noni) have gained considerable popularity and are sold worldwide as food supplements and novel foods, mostly via the internet. Current opinions regarding the value of noni products differ considerably and range from very positive [7] to highly critical [8] or cautious [9]. The extraordinary transformation of noni from a Polynesian ethnomedicine to a commercial food supplement with a wide spectrum of health-related claims was probably spurred by a publication in 1985 in the Pacific Tropical Garden Bulletin [10], in which the author claimed the presence of an active "alkaloid" named xeronine. This compounds, for which no structure was given, was said to derive from a precursor,

proxeronine. The author described a wide range of potential indications for Noni juice including "high blood pressure, menstrual cramps, arthritis, gastric ulcers, sprains, injuries, mental depression, senility, poor digestion, atherosclerosis, blood vessel problems, drug addiction, relief of pain and many others."

Noni products have been commercialized in the USA since the 1990s and are nowadays available in health food stores and on the internet ^[11]. Products derived from leaves and fruits are being sold as capsules, teas, and as juice, the fruit juice being the predominant form. Juices may be pasteurized or obtained by fermentation process; some of the noni juices are flavoured by addition of other fruit juices to render the product more palatable. The popularity Of Noni products in the USA has been attributed to claims of a "cureall" for a variety of diseases. Noni fruit juice is legally sold in European Community since 2003, and other products are readily available on the internet. Reliable sale figures are not available, but it is claimed that the market has reached US \$ 1.3 billion in annual sales.

Morinda citrifolia L. belongs to the family Rubiaceae. The genus Morinda comprises some 80 species which all occur exclusively in tropical climate zones [12]. M. citrifolia is an evergreen tree or shrub 3 to 6 m high, with bright green ovate and deeply veined leaves which are 10 to 30 cm long. The tubular flowers are white. The unusual fruit has an ovoid shape covered by polygonal-shaped sections. It reaches a length of up to 12cm and has the size of a potato. The immature fruit is hard and has a bright green colour. Upon ripening, the fruits become very soft and turn to a translucent yellowish or white. The ripe fruit has an unpleasant butyric and cheesy odour and soapy taste. The seeds are buoyant due to an air sac attached at one end and may germinate even after extended periods of drifting in the sea. This explains, in part, the wide distribution of the noni tree in the Indo-Pacific Islands which was further favoured by the migration of seafaring Polynesians. Morinda citrifolia occurs from India through Southeast Asia and Australia to Eastern Polymesia and Hawaii. More recently, the plant has been introduced to other regions with tropical climates. Commonly used vernacular names are "Indian Mulberry". "Noni" and "Nonu"; in Australia, the fruit is commonly known as "cheesefruit".

Morinda citrifolia has a long tradition as a medicinal plant in India and the Pacific Islands. All parts of the plants have been used including leaf, fruit, roots, bark, flower and seed. Typical uses have been reported as a treatment of boils and curs, abscesses, and inflammations of various origins, fungal infections, constipation as well as diarrhoea. Root and bark of the noni tree have been used as natural yellow and red dyes, due to their content in anthraquinones. Ethnobotanical investigations on the dietary habits of aboriginal populations of Polynesia and Australia report on raw or cooked noni fruit. However, its consumption was apparently limited to times to famine due to the unpleasant taste and flavour of the ripe fruits.

To satisfy the increasing demand for noni products, cultivation has been established in Polynesia and Hawaii. M. citrifolia is relatively easy to propagate, either from seeds or from cuttings. The tree grows at altitudes up to 400m and is fairly undemanding once mature. Noni plants begin to bear fruits already one year after planting. Mature trees typically produce 120-250kg of fruits per year. In Hawaii, average annual yields of 50 t per hectare are achieved [13]. Considering a 60% extraction rate, this would correspond to an annual production of 30 t of juice per hectare. Even though noni farming seems profitable, it is no match to the staggering profits achieved at the wholesale and retail levels if one considers the current pricing of noni products [14]. Noni juices are prepared by a variety of methods. Traditionally, mature noni fruits are fermented in a collection vessel and the juice collected by drip-extraction. Non-fermented juices are obtained by squeezing or pressing mature fruits and preservation by pasteurization. Solid dosage forms such as capsules contain a powder obtained by evaporation of the juices and addition of non-hygroscopic excipients to avoid clumping of the highly hygroscopic dry extract [14].

Uses of Noni Fruit

Noni has traditionally been used for colds, flu, diabetes, anxiety, and high blood pressure, as well as for depression and anxiety. All plant parts are used for a variety of illnesses in Samoan culture, and noni is one of the most frequently used Hawaiian plant medicines. Claims that have not been proven in clinical trials include: the use of bark for the treatment of bacterial infections, cough, diarrhea in infants, and stomach ailments; the flowers for sore or irritated eyes, styes, conjunctivitis, ocular inflammation, and coughs; the fruit for asthma, wounds, broken bones, mouth and throat infections, tuberculosis, worms, diarrhea, fever, vomiting, eye ailments, arthritis, depression, seizures, bacterial and fungal infections, viruses, and as a tonic; the fresh fruit juice for cancer; the dried leaves used externally for infections, burns, children's chest colds,

and inflammation, and internally for boils, pleurisy, inflamed gums, and arthritic pain; the fresh leaves used externally for burns and internally for fevers, hemorrhage, bacterial infections, and inflammation; and the roots for oral ulcerations, fevers, and cancerous swellings.

Phytochemistry of Noni fruit

Early phytochemical investigations on M. citrifolia focussed on secondary metabolites in leaves, roots and bark. The roots contain a wide spectrum of anthraquinones such as rubiadin, damnacanthal and alizarin-1-methyl ether, naphthoquinone derivatives and sterols ^[15], whereas several iridoids, flavonol glycosides and triterpenes were reported from the leaves ^[16]. Plant cell cultures were analysed mainly for their capabilities for synthesis of anthraquinoid pigments. The interest in the constituents of the fruit was stimulated by the introduction of fruits juices as food supplement. Up to now, several classes of metabolities have been described, including polysaacharides, fatty acid glycosides, iridoids, anthraquinones, coumarins, flavonoids, lignans, phytosterols, carotinoids, and a range of volatile constituents including monoterpenes and short chain and fatty acids and fatty acid esters.

Nutritional composition of unfermented noni juice has been analysed. It contains approx. 10% of dry matter consisting mainly of glucose and fructose (3-4% each), protein (0.2-0.5%) and lipids (0.1-0.2%). The content in potassium is relatively high (3.-150ppm), followed by calcium, sodium and magnesium. Vitamin C contents reported varied from 30-150mg/kg [17,18]. The polysaccharide fraction consists primarily of the pectins homogalacturonan, rhamnogalacturonan I, arabinan, and type I and II arabinogalactans [19].

Among the phytochemicals reported so far in the fruits the fatty acid glycosides and alcohols appear quite unique with respect to their structures and content in ripe fruits [20-23]. They consist of one, occasionally two short-chain fatty acids, or an alcohol attached to a sugar moiety consisting of one to three glucoses. Due to their structure, they possess more or less pronounced amphiphilic properties and may be, at least in part, responsible for the soapy taste of ripe fruits.

Noni fruit contains numerous iridoids. Main compounds are asperuloside [24], asperulosidic acid and deacetylasperulosidic acid [25]. Minor iridoids include deacetylasperuloside, dehydromethoxygaertneroside, epi-dihydrocornin, 6 alpha-hydroxyadoxoside, citrifolinin B epimers a and b, and 6b,7beta-epoxy-8-epi-splendoside [26]. A number of other compounds classes have been reported. Flavonol glycosides include rutin, narcissoside and nicotifloroside. Several known and new lignans such as 3,3'-bisdemethylpinoresinol, americanol A, americanin A, americanoic acid A, morindolin, isoprincepin [27] and balanophonin [28] have been isolated. The coumarin scopoletin has been identified. Similar to other parts, the fruits also contain a wide spectrum of 1-hydroxyanthraquinones, albeit in much lower concentrations. These include new compounds such as 2-methoxy-1,3,6-trihydroxyanthraquinone, and 5,15-dimethylmorindol. Finally, miscellaneous compounds such as beta-sitosterol and its 3-O-glucoside, ursolic acid and 19-hydroxyursolic acid, cytidine, borreriagenin and epiborreriagenin, iridoid derivative, succinin acid diesters, 4-hydroxy-3-methoxycinnamaldehyde, beta-hydroxypropiovanillone and vanillin have been isolated. Morindacin, previously reported as a new iridoid from noni fruit was recently shown to be identical with borreriagenin [29]

The characteristic cheesy smell of mature noni fruits instigated the study of the volatile components collected by solvent extraction, stem distillation or solid phase microextraction (SPME). Major volatile compounds were octanoic and hexanoic acids, and 3-methyl-3-buten-1-ol. Minor compounds include free fatty acids, alcohols, aldehydes and ketones, esters, traces of monoterpenes, and a series of sulphur compounds [30,31]. Unripe fruits contain mainly C16 and C18 fatty acids, whereas fatty acids of shorter chain length are dominant in ripe fruits and are mainly responsible for their unpleasant cheese-like flavour.

With the exception of a preliminary study [32], no methods for the control of authenticity and quality of noni products have been published up to now. The authors used planar chromatography for non-volatile compounds and headspace solid-phase microextraction (HS-SPME) GC-MS for analysis of volatile constituents. Chemometric data treatment revealed distinct differences in samples originating from Hawaii and Cook Islands, Tahiti, and of noni juices mixed with other fruit juices.

Pharmacology

A growing number of pharmacological studies on noni juice and isolated compounds from the fruit have been published in recent years. They are chiefly related to three areas: cancer, inflammation and metabolic diseases. Many of the reports are only available as congress abstracts and not (yet) as peer-reviewed research papers. Hence, the quality of the data and significance of findings cannot be fully assessed in these cases.

Fatty acid glycoside 1 and an iridoid, asperulosidic acid, were found to inhibit phorbol ester- and EGF-induced AP-1(transcription activator protein-1) transactivation and cell transformation in mouse epidermal JB6 cells ^[33]. A polysaccharide-rich fraction, which was obtained from fruit juice by precipitation in ethanol, showed anti-tumor activity in the Lewis lung carcinoma model in mice. The precipitate also stimulated the release of certain cytokines such as TNF- alpha, IL-1beta, IL-10, and IF- gamma, but not of IL-2 ^[34]. In a similar study, the precipitate showed anti-tumor activity against Sarcoma 180 ascites tumor in mice ^[35]. However, it should be mentioned that these two murine tumor models have been abandoned by the National Cancer Institute (NCI) many years ago in favour of human xenografts in nude mice.

reportedly preventive effect the Noni fruit had initiation stage 7,12dimethylbenz[a]anthracene(DMBA)-induced mammary breast carcinogenesis in rats [36]. In similar study using the same model, a synergistic effect of fruit juice and methylsulphonylmethane was observed [37,38]. The juice also showed antimutagenic activity in ICR mice [39]. Anthraquinone 31 was identified as a potent inducer of quinone reductase activity, with a 40-fold higher potency than the well-known inducer sulforaphane. There was no discernible cytotoxicity at the highest dose tested. Noni juice, at a concentration of 5%, strongly inhibited the initiation of new vessel sprouts from a model of placental vein explants. At a concentration of 10%, vessel degeneration and apoptosis in established capillary networks were observed. This concentration was effective at inhibiting capillary initiation in explants from human mammary tumors, and led to degeneration of vessels in explants showing capillary sprouting [40]. Growth inhibition of breast cancer and neuroblastoma cell lines in vitro was reported for a methanolic extract from fruits at a concentration of 0.1mg/ml, whereas non-cancerous cells were not inhibited at this concentration [41]. It should be noted, however, that the concentration used in these experiments were high.

Noni fruit juice extract showed anti-inflammatory activity in the carrageenan-induced rat paw oedema when 10 or 200mg were administered intraperitoneally. These doses were also effective in reducing the bradykinin-induced oedema in the rat paw [42]. Oral dosage of juice to neonatal equine foals (60ml twice daily) was found to reduced the expression of COX-2 and several cytokines in LPS-stimulated monocytes in an ex vivo experiment. However, the number of animals was not sufficient for statistically significant findings [43]. An anthraquinone isolated from noni fruit reportedly inhibited matrix metalloproteinase-I in primary cultures of human fibroblasts. In nude mouse skin, the compound increased the dermal type-I procollagen [44].

Noni juice reportedly lowered serum cholesterol and triglycerides in smokers ^[45]. In male adult Sprague-Dawley (SD) rats, an antithrombotic effect on jugular vein thrombosis induced by ferric chloride was observed ^[46]. A fruit extract showed antioxidative activity in several in vitro test systems ^[47]. Antioxidant activity of americanin from a noni fruit extract against 1,1-diphenyl-2-picrylhydrazyl (DPPH) and peroxynitrite radicals was reported.

Potential antidiabetic and hepatoprotective properties have been investigated. Noni fruit extract reportedly inhibits phosphodiesterase 3 and shows agonistic activity at the P2Y receptor ^[48]. A protective effect against carbon tetrachloride-induced live injury in female SD rats has been described ^[49].

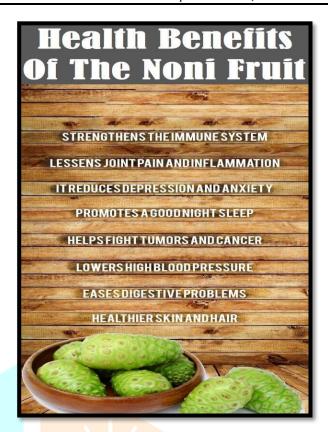


Figure: Health Benefits of Noni Fruit

Information on clinical studies

Testimonials on health beneficial properties of noni abound on countless internet sites. Clinical data published in the scientific literature, however, are still scant. In two case reports a significantly prolonged survival of cancer patients taking noni juice was claimed [50]. Of significantly higher interest is a phase I clinical trail sponsored by the National Centre for Complementary and Alternative Medicine (NCCAM) of the National Institute of Health (NIH). It was initiated in 2001 at the Cancer Research Centre of Hawaii, Honolulu. Some information on the aims of the study can be found at the website of the center [51] and on the website of NIH sponsored clinical trails [52]. The hypothesis being tested is that noni, at a specified dosing, provides cancer patients with a sufficient benefit to toxicity profile to be useful as a therapeutic. Principal aims at this point are to determine the maximum tolerated dose of a freeze-dried noni fruit extract, to assess possible toxicities associated with the treatment, collect preliminary information on efficacy in tumour and symptom control, and identify of marker compounds for bioavailability and pharmacokinetics. Recently, preliminary data from the trail were reported. Toxicity and quality of life measures were assessed. A statistically significant decrease in pain interference with activities was observed, and a non-significant but consistent dose response effect for global health status. No tumour regression was noted [53]. According to the principal investigator, over 50 patients have entered the study at different dose levels which should be completed in 2007. The dose providing maximum quality of life should be identified in this phase I trial, to be used subsequently in a phase II efficacy study (B. Issell, personal communication).

Patenting activities

A considerable number of patent applications have been filled in recent years, mainly by businesses commercializing Noni-based products. Chiefly, the claims extend to anticancer, anti-metastatic and cancer preventive properties, involving among others, aromatase inhibition and anti-angiogenetic effects ^[54-59]. Use of noni based products as antifungals, including treatment of candidiasis has been claimed ^[60,61]. A third category of patents relates to rather general protective properties against cell damage ^[62].

Legal status of Noni products

Noni juice has been marketed in the USA since 1July 1996 as a dietary supplement, as well as in Canada, Japan, Australia, Mexico, Norway and Hong Kong. Noni based products had no previous history of use in Europe. Therefore, distribution in countries of the EC required an approval either as drug or as food. The

manufacturer of Tahitian Noni filed an application for approval as Novel Food which was granted by the European Commission in 2003 ^[63], on the basis of a report by the scientific committee on food of 1 December 2002 ^[64]. The expert committee, however, noted that the recommended daily intake of 30ml was rather uncommon for a fruit juice. The approval applies only to the juice of noni fruit and not to other types of noni products such as, for example, those based on dry extracts from fruits and leaves. Such preparations seem increasingly popular if one considers the range of products available in the USA. Some of these preparations are distributed in Europe via internet sales. As per October 2005, the European Commission has received over 25 notifications for noni juice as a novel food ingredient on the basis of a claimed equivalence.

Safety of Noni fruits

A Comprehensive review of safety aspects, including data from internal laboratory reports, has been recently published ^[65]. Neither in acute, subacute, nor sub-chronic testing in rats were signs of toxicity observed ^[66]. The LD50 values of intraperitoneally injected aqueous and alcohol extracts were found to be 7500 mg/kg and 3500 mg/kg body weight, respectively, in mice. This is in accord with previous reports of an LD50>1000 mg/kg in mice for an intraperitoneally injected methanolic extract of the fruit. Oral toxicity tests with Tahitian Noni juice revealed no adverse effects at doses equivalent to 80 ml/kg body weight per day in rats. Assessment of genotoxicity in various in vitro and in vivo models did not reveal a genotoxic risk.no allergenic response was observed in guinea pigs when noni juice was administered by gavage, intraperitoneal and intravenous application routes.

In 2005, two clinical case reports were published which associated consumption of noni juice with three cases of acute hepatitis in Austria. While two patients recovered spontaneously after ceasing of intake, the third patient underwent liver transplantation. On 6 March 2006, the German Office for Risk Assessment (BfR) issued information on potential health risks related to consumption of noni products. According to this document, a case of liver inflammation in relation to consumption of noni juice has been reported in Germany. Details on this case were published recently: the patient who was treated with interferon-beta because of multiple sclerosis admitted to use noni juice for "general immune system stimulation". She showed elevated transaminase and bilirubin levels which did not decrease after cessation of interferon-beta administration, but were normalized after stopping drinking noni juice. However, the apparent causality of noni juice has been recently contested by Tahitian Noni International, which concludes to a case of persisting interferon-beta hepatotoxicity. A causal link of noni intake and observed hepatotoxicity has also been questioned for the previously reported cases. In recent publication, data from a single-center, double-blind, placebo-controlled safety study with three dose levels of noni juice were discussed. According to this account, a daily dose of 750 ml for 28 days had no measurable effect on clinical parameters of liver function, on blood cell counts and serum chemistry. The authors also describe data from unpublished animal toxicity study in rats for determination of the "no observable adverse effect level" (NOAEL), which was determined to be >80 ml/kg day. They argue that the ingested doses in the three cases of hepatoxicity were 10 to 80 folds lower than the NOAEL and that the hepatotoxic reactions could, therefore, not be caused by noni juice. At the same time, in a study reviewing the use of herbal products by patients with stage 5 chronic kidney disease, the author cautioned that dialysis patients should avoid noni juice because of its high potassium content.

The approval by the European Community of noni juice as a Novel Food in 2003 was, among others, based on a review of the toxicological data available at that time. In consideration of the reported cases of hepatotoxicity, the European Community requested the European Food Safety Authority (EFSA) to review the scientific elements and to consider whether the current status would need to be amended. The report adopted on 1 September 2006. Concluded that there was no convincing evidence for a causal relationship between the hepatoxicity described in the clinical case reports and the consumption of noni juice. A possible link between anthraquinones in noni juices and hepatotoxic reactions, as suggested in the clinical case reports, was excluded in the EFSA report. While the anthraquinone content is relatively high in the roots (in earlier times, they were used for this reason as a natural red or yellow dye) their concentration in the fruits seems to be extremely low.



Figure: Morinda Citrifolia (Noni) Fruit

Current Status and Future Prospects

Current Status of nutraceuticals:

Nutraceutical food or food components that help in treatment and prevention of diseases are made from herbal/botanical raw material. This is rapidly growing industry (7-12% per year) with more than millions of people in the world using these natural products. The global nutraceutical market to reach \$ 450 billion by 2015. According to recent analysis from Euro monitor, international global sales of health and wellness products are on track to reach a record of about \$ 1 trillion by 2017, fueled by functional/fortified products designed to offer specific health benefits.

The Indian consumer's awareness about conventional nutraceutical ingredients is severely limited and nutraceutical manufacture's need to take up the cause and spread awareness about their products to the Indian masses. The global nutraceutical market has seen maximum growth in last decade. In India, beverages and functional food are expected to witness much higher growth rates when compared to dietary supplement over the next five years.

In the Asia Pacific nutraceutical product market, Japan represents the largest consumer, followed by China. India's functional food market is forecast to record moderate growth, with functional foods and beverages forecast to account for almost 71% of the dietary supplement sector in 2017. In Middle East and Africa, dietary supplements represent the fastest growing market segment in the nutraceutical market, recording almost 31% yearly growth between 2007 and 2011.

Table: Nutraceuticals with Their Therapeutic Benefits

Name of Nutraceutical	Therapeutic Benefits
Natural Lycopene	Reducing risk of prostate and cervical
	cancers.
	Supporting cardiovascular health.
Natural purified Lutein Esters	Dietary supplement
	Functional foods antioxidants.
Garlic	Cholesterol lowering
	Cardiac diseases
	Diabetic support
Green Tea	Cancer prevention
	Weight management
	Lowering cholesterol
Gymnema, Momordica	Diabetic control
Glucosamine	Arthritis treatment
Ginkgo Biloba	Allergy relief
Digestive Enzymes	Digestive Support
Ginseng	Immunomodulator
Phycocyanin	Antioxidant

Future Prospects of Nutraceuticals:

Nutraceuticals are products formed as a result of combined efforts of food, pharmaceutical and chemical industries. Botanical dietary supplement segment is anticipated to witness considerable growth over the forecast period of five years on account of increasing risk of various life style ailments like obesity, hypertension, diabetes, etc. Rapidly expanding nutraceutical market is indicating the emergence of a new era in health and wellness industry. Inclination from pharmaceuticals to nutraceuticals indicates the shifting trend in health care sector. Tremendous growth in nutraceutical industry has implications for food, pharmaceutical and agriculture sector. According to a latest research report by Grand View Research, nutraceutical market is projected to reach worth USD 578.23 Billion with CAGR of 8.8% by 2025.

Conclusion

Nutraceuticals are widely used in the food and pharmaceutical industries. Most of the nutraceuticals are from either mineral origin, animal origin or vegetable origin like gamma terpenes, beta carotene, curcumins, limonene, eugenol, pinene, safranal, geraniol, aloine, caryophyllene, lycopene and silymarin. These constituents are prepared into dosage forms as topical, oral, etc. viz. creams, lotions, ointments, emulsions, unani formulations, aromatic oils, microemulsions, SMEEDS, breads, tablets, emulgels, herbal formulations etc. used in various categories as antidiabetic, antibiotic, antimicrobial, anti-inflammatory, anti-cancer, protective, etc. Nutraceuticals are quickly replacing pharmaceuticals in prevention and management of acute and chronic health problems. Nutraceuticals show an ample scope to flourish in future as therapeutic agents with preventive and curative properties.

The number of scientific publications on noni fruit has been rapidly growing over the past few years, but the current state of knowledge is still far from satisfactory. First of all, a comprehensive phytochemical profiling is needed to provide sufficient qualitative data on the chemical composition. Secondly, tools for appropriate quality assessment of noni products are lacking. Validated analytical methods are required for a comparative assessment of noni products and for quantitative determination of important marker and/or putative bioactive compounds. Given that the noni market is largely uncontrolled, a survey of the quality of available products is desirable from a perspective of consumer safety. Pharmacological studies of high quality are needed to shed light on putative modes of action. Past investigations on pharmacological properties of noni juice and purified compounds have been mostly at the in vitro level and, quite often, with rather high concentrations. Some of the in vivo experiments have been using animal models which are no longer state-of-the-art. A large number of the pharmacological studies have been published only as congress abstracts and not yet as peer-reviewed research publications. Hence, the quality of these data cannot be adequately assessed. However, some interesting activities such as chemo-preventive and anti-angiogenic properties warrant further

investigation. To what extent the findings from the experimental pharmacological studies are of potential clinical relevance is not clear for the moment. There is a stark contrast between the sweeping claims on curative and disease preventive properties of noni products and testimonials published on numerous websites, on one hand, and the almost complete lack of clinical data on the other. In that respect, the publication of a full account on the NIH-sponsored phase- I clinical study will be of major importance. The issue of potential hepatoxicity needs to be followed up by further studies since noni juice is sold in Europe as a food item. The adverse events seem rare and may be idiosyncratic in nature. While the causality of noni consumption in the reported cases is doubtful, the current lack of conclusive evidence of clinically relevant benefits has to be taken into account in the risk assessment.

References

- 1- Kalra EK, Nutraceutical Defination and introduction. AAPS Pharm Sci. 2003;5:E25.
- 2- Chauhan B, Kumar G, Kalam N, Ansari SH, Current concepts and prospects of herbal nutraceutical: A review. J Adv Pharm Technol Res. 2013;4:4-8.
- 3- Zeisel SH, Regulation of "nutraceuticals" Science. 1999;285:1853-5.
- 4- Hardy G, Nutraceuticals and functional foods: Introduction and meaning. Nutrition. 2000;16:688-9.
- 5- https://jbkwellnesslabs.com
- 6- https://www.onlymyhealth.com
- 7- Wang MY, West BJ, Jensen CJ, Nowicki D, Su C, Palu AK et al. Morinda citrifolia (Noni): a literature review and recent advances in Noni re- search. Acta Pharmacol Sin 2002; 23: 1127-41.
- 8- Seidemann J. Noni: Fragwürdige Zauberfrucht aus der Südsee. Pharm Z 2001; 146: 36-40.
- 9- McClatchey W. From Polynesian healers to health food stores: chan- ging perspectives of Morinda citrifolia (Rubiaceae). Integr Cancer Ther 2002; 1: 110-20.
- 10- Heinicke RM. The pharmacologically active ingredient of Noni. Pacific Trop Bot Gard Bull 1985; 15: 10-4.
- 11-Dixon AR, McMillan H, Etkin NL. Ferment this: the transformation of Noni, a traditional Polynesian medicine (Morinda citrifolia, Rubia- ceae). Econ Bot 1999; 53: 51-68.
- 12-Morton JF. The ocean-going Noni, or Indian mulberry (Morinda citrifolia, Rubiaceae) and some of its "colourful" relatives. Econ Bot 1992; 46: 241-56.
- 13-Nelson SC. Noni cultivation in Hawaii. Fruits and Nuts 2001; 4: 1-4.
- 14- Nelson SC. Noni cultivation and Production in Hawai'i. In: Proceedings of the 2002 Hawai'i Noni Conference 2003. Nelson SC, editor. University of Hawaii at Manoa: College of Tropical Agriculture and Human Resources; 2003: 33-50.
- 15-Sang S, Ho CT. Chemical components of Noni (Morinda citrifolia L.) root. ACS Sym Ser 2006; 925: 185-92.
- 16-Sang S, Wang M, He K, Liu G, Dong Z, Badmaev V et al. Chemical components in noni fruits and leaves (Morinda citrifolia L.). ACS Sym Ser 2002; 803: 134-50.
- 17-Scientific Committee on Food Opinion of the Scientific Committee on Food on Tahitian Noni® juice. Available at http://europa.eu.int/comm/ food/fs/sc/scf/out 151_en.pdf. Expressed December 4 2002 in Brussels.
- 18- Shovic AC, Whistler WA. Food sources of provitamin A and vitamin C in the American Pacific. Trop Sci 2001; 41: 199-202.
- 19-Bui AKT, Bacic A, Pettolino F. Polysaccharide composition of the fruit juice of Morinda citrifolia (Noni). Phytochemistry 2006; 67: 1271-5.
- 20-Wang M, Kikuzaki H, Csisar K, Boyd CD, Maunakea A, Fong SFT et al. Novel trisaccharide fatty acid ester identified from the fruits of Morinda citrifolia (Noni). J Agric Food Chem 1999; 47: 4880-2.
- 21-Wang M, Kikuzaki H, Jin Y, Nakatani N, Zhu N, Csiszar K et al. Novel glycosides from noni (Morinda citrifolia). J Nat Prod 2000; 63: 1182-3.
- 22- amoylenko V, Zhao J, Dunbar DC, Khan IA, Rushing JW, Muhammad I. New constituents from Noni (Morinda citrifolia) fruit juice. J Agric Food Chem 2006; 54: 6398-402.

- 23-Dalsgaard PW, Potterat O, Dieterle F, Paululat T, Kühn T, Hamburger M. Noniosides EH, new trisaccharide fatty acid esters from the fruit of Morinda citrifolia (Noni). Planta Med 2006; 72: 1322-7
- 24-Levand O. Larson HO. Some chemical constituents of Morinda citrifolia. Planta Med 1979; 36: 1867.
- 25- Kamiya K, Tanaka Y, Endang H, Umar M, Satake T. New anthraquinone and iridoid from the fruits of Morinda citrifolia. Chem Pharm Bull 2005; 53: 1597-9.
- 26-Su BN, Pawlus AD, Jung HA, Keller WJ, McLaughlin JL, Kinghorn AD. Chemical constituents of the fruits of Morinda citrifolia (Noni) and their antioxidant activity. J Nat Prod 2005; 68: 592-5.
- 27- Kamiya K, Tanaka Y, Endang H, Umar M, Satake T. Chemical constitu- ents of Morinda citrifolia fruits inhibit copper-induced low-density li- poprotein oxidation. J Agric Food Chem 2004; 52: 5843-8.
- 28-Pawlus AD, Su BN, Keller WJ, Kinghorn AD. An anthraquinone with po-tent quinone reductase-inducing activity and other constituents of the fruits of Morinda citrifolia (Noni). J Nat Prod 2005; 68: 1720-2.
- 29-Schripsema J. Caprini GP, Dagnino D. Revision of the structures of ci- trifolinin A, citrifolinoside, yopaaoside B, and morindacin, iridoids from Morinda citrifolia L and Morinda coreia Ham. Org Lett 2006; 8: 5337-40.
- 30-Farine JP, Legal L, Moretau B, Le Quere JL. Volatile components of ripe fruits of Morinda citrifolia and their effects on Drosophila. Phytochem-istry 1996; 41: 433-8.
- 31- Wei GJ, Huang TC, Huang AS, Ho CT. Flavor compounds of Noni fruit (Morinda citrifolia L) juice. ACS Sym Ser 2004; 871: 52-61.
- 32-Lachenmeier K, Musshoff F, Madea B, Reusch H, Lachenmeier DW. Au- thentication of Noni (Morinda citrifolia) juice. Dtsch Lebensmitt Rundsch 2006; 102: 58-61.
- 33-Liu G, Bode A, Ma WY, Sang W, Ho CT, Dong Z. Two novel glycosides from the fruit of Morinda citrifolia (Noni) inhibit AP-1 transactivation and line. Cancer Res 2001; 61: 5749-56.
- 34-Hirazumi A, Furusawa E. An immunomodulatory polysaccharide-rich substance from the fruit juice of Morinda citrifolia (Noni) with antitu- mor activity. Phytother Res 1999; 13: 380-7.
- 35-Furusawa E, Hirazumi A, Story S, Jensen J. Antitumor potential of a polysaccharide-rich substance from the fruit juice of Morinda citrifolia (Noni) on sarcoma 180 ascites tumor in mice. Phytother Res 2003; 17: 1158-64.
- 36-Wang MY, Anderson GL, Nowicki D. Preventive effect of Morinda citrifolia (Noni) at the initiation stage of mammary breast carcinogen- esis induced by 7,12-dimethylbenzo(a)anthracene (DMBA) in female Sprague-Dawley (SD) rats. Cancer Epidemiol Biomark Prev 2002; 11: 1218S.
- 37- Wang MY, Su C. Cancer preventive effect of Morinda citrifolia (Noni). Ann NY Acad Sci 2001; 952: 161-8.
- 38-Wang MY, Anderson GL, Nowicki D. Synergistic effect of Tahitian noni juice (TNJ) and methylsulfonylmethane (MSM) on mammary breast cancer prevention at the induction stage of chemical carcinogenesis induced by DMBA in female Sprague-Dawley (SD) rats. Cancer Epide-miol Biomark Prev 2003; 12: 1354S.
- 39-Nowicki J, Haun J. Peng L, Anderson G, Nowicki D, Wang MY. Antimu-tagenic activity of Morinda citrifolia (Noni) fruit juice in ICR mice. Can-cer Epidemiol Biomark Prev 2005; 14: 16895.
- 40-Hornick CA, Myers A, Sadkowska-Krowicka H, Anthony CT, Woltering EA. Inhibition of angiogenic initiation and disruption of newly estab- lished human vascular networks by juice from Morinda citrifolia (Noni). Angiogenesis 2003; 6: 143-9.
- 41- Arpornsuwan T, Punjanon T. Tumor cell-selective antiproliferative effect of the extract from Morinda citrifolia fruits. Phytother Res 2006; 20:515-7.
- 42-McKoy MLG, Thomas EA, Simon OR. Preliminary investigation of the anti-inflammatory properties of an aqueous extract from Morinda citrifolia (Noni). Proc West Pharmacol Soc 2002; 45: 76-8.
- 43- Xu J, McSloy AC, Anderson BK, Goodbee RG, Peek SF, Darien BJ. Tahitian Noni Equine Essentials TM: a novel anti-inflammatory and COX-2 inhibitor which regulates LPS induced inflammatory mediator expres-sion in equine neonatal monocytes. J Vet Intern Med 2006; 20: 756.

- 44- Kim SW, Jo BK, Jeong JH, Choi SU, Hwang YI. Induction of extracellular matrix synthesis in normal human fibroblasts by anthraquinone isolated from Morinda citrifolia (Noni) fruit. J Med Food 2005; 8:552-5.
- 45-Wang MY, Henley E, Nolting J, Cheerva A, Jensen J, Anderson G et al. The effects of Morinda citrifolia (Noni) fruit juice on serum cholesterol and triglyceride in current smokers. Circulation 2006; 113: E327.
- 46-Ayanbule F, Wang MY, Peng L, Nowicki J, Anderson G, Nowicki D. An-tithrombotic effect of Morinda citrifolia (Noni) fruit juice on the jugu- lar vein thrombosis induced by ferric chloride in male adult SD rats. Arterioscler Thromb Vasc Biol 2006; 26: E104.
- 47-Zin ZM, Abdul-Hamid A, Osman A. Antioxidative activity of extracts from Menkudu (Morinda citrifolia L) root, fruit and leaf. Food Chem 2002; 78: 227-31.
- 48- Su CX, Jensen JC, Zhou BN. Morinda citrifolia (Noni): its effect on insu- lin secretion by G-protein-coupled receptor systems. San Diego, CA:229th ACS National Meeting; 2005.
- 49-Wang MY, Anderson GL, Nowicki D. Jensen J. Protective effect of Morinda citrifolia (Noni) fruit juice against chronic liver injury in- duced by carbon tetrachloride in female SD rats. Cancer Epidemiol Biomark Prev 2004; 13: 18385.
- 50- Wong DKW. Are immune responses pivotal to cancer patient's long term survival? Two clinical casestudy reports on the effects of Morinda citrifolia (Noni). Hawaii Med J 2004; 63: 182-4.
- 51- The Noni study Available at http://www.crch.org/CenStudyNoni.htm. Accessed in 2006.
- 52-Clinical trial: study of Noni in cancer patients. Available at http://www.clinicaltrials.gov/show/NCT00033878. Accessed in 2006.
- 53-Issell BF, Gotay C, Pagano I, Franke A. Quality of life measures in a phase I trial of noni. J Clin Oncol 2005; 23: 7825.
- 54-Ghai G, Ho CT, Rosen RT, Wang M, Boyd CD, Csiszar K. Glycosides from Noni extract for treatment of tumours. US Patent Application 2002- 150213; 2003.
- 55- Jensen CJ, Palu AK, Story SP, Jensen S, Su C. Preventative and treatment effects of Morinda citrifolia as a colon cancer cell growth inhibitor. US Patent Application 2002-285334; 2003.
- 56-Jensen CJ, Palu AK, Lemus D, Fuenzalida M, Mihovilovic D. Anti-angio- genesis effects of Morinda citrifolia. US Patent Application 2002- 286112; 2004.
- 57-Palu AK, West BJ, Jensen CJ, Su C, Zhou BN, Story SP. Preventative and treatment effects of Morinda citrifolia as an aromatase inhibitor. US Patent Application 2004-192 761; 2004.
- 58-Su C, West B, Palu A, Hirasumi-Kim A, Jensen CJ, Story S. Morinda citrifolia-based formulation for inhibiting metastasis of carcinogenic cells. PCT International Application WO 2004 098 514; 2004.
- 59- Wang MY, Jensen CJ, Su C. Preventative effects of Morinda citrifolia on mammary breast cancer. US Patent Application 2005-037101; 2005.
- 60- West BJ. Jensen CJ, Palu AK, Ogden RV, Gerson S. Method and formula- tion for treating candidiasis using Morinda citrifolia. US Patent Appli- cation 2002-294089; 2003.
- 61-Gerson S, Palu AK, Zhou BN, Su C, Jensen CJ, Story SP et al. Antifungal effects of Morinda citrifolia. US Patent Application 2003-439596; 2003.
- 62-Su CX, Jensen CJ, Story SP. Morinda citrifolia juice dietary supplement for reducing cellular damage in the human body. PCT International Application WO 2001-US47203; 2002.
- 63-European Commission, Commission Decision of 5 June 2003 authoris- ing the placing on the market of "noni juice" (juice of the fruit of Morinda citrifolia L) as a novel food ingredient under Regulation (EC) Nr. 258/97 of the European Parliament and of the Council. Official Journal of the European Union 2003; L 144/12: 12.6.2003.
- 64-European Commission Health & Consumer Protection Directorate- General. Opinion of the Scientific Committee on Food on Tahitian Noni® juice. Available at http://europa.eu.int/comm/food/fs/sc/scf/index_en.html. Accessed on December 11, 2002.
- 65- West BJ, Jensen CJ, Westendorf J. White LD. A safety review of Noni fruit juice. J Food Sci 2006; 71: R100-6.
- 66-Mancebo A, Scull I, Gonzalez Y, Artega ME, Gonzales BO, Fuentes D etal. Ensayo de toxicidad a dosis repetidas (28 dias) por via oral del ex-tracto acuoso de Morinda citrifolia en ratas Sprague Dawley. Rev Toxi- col 2002; 19: 73-8.