

Polynesian ethnobotanicals: a critical role in new drug discovery

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Introduction

Extracts of plants from Polynesian sources, particularly plants indigenous to the Hawai'ian islands, have been used for centuries to assist in the treatment of a wide variety of diseases. Over the last few years, preparations from plants such as noni (*Morinda citrifolia*) have appeared in abundant quantities in the rapidly expanding herbal market in North America and Europe. The health related claims associated with these plant extracts, however, are almost entirely unsupported by any legitimate scientific evidence and considerable care needs to be taken to explore both the biological and clinical effects of these extracts if the full clinical potential of Polynesian ethnobotanicals is to be realized.

For over a millenium, Hawai'ian medical practitioners and herbalists (or *kāhuna lā'au lapa'au*) have used a wide variety of Polynesian plants introduced into the Hawai'ian islands to treat diseases ranging from stomach ulcers and urinary disorders to skin infections.¹ Indeed, prior to the late 1700s when the indigenous Hawai'ian people were first exposed to the many infectious diseases carried by European sailors, *kāhuna* in Hawai'i had developed clinical practices involving these plant extracts for patient care in an organized Hawai'ian society whose medical management matched that in any society of that time.²

The holistic views and ethnomedical practices of the Hawai'ian *kahuna* are continued today through the services of a small number of traditional healers who base their

training on the healing practices of the Hawai'ian *kupuna* (elders) and their largely oral traditions of medical practice.³ Possibly the best known of these traditional healers is Henry Papa Auwae, an herbalist who recognizes that a legitimate practitioner of Hawai'ian ethnomedicine relies on both a spiritual and an ethnobotanical contribution to healing (ref.3 and Henry Auwae, personal communication).

Ethnobotanicals in Hawai'i

Over the last decade, there has been increased interest by the medical and pharmaceutical communities in the United States in the ethnobotanical component of traditional healing practices in a number of different ethnic communities, including Hawai'i. This increased interest originates from the possibility that these extracts may provide new and effective alternatives to pharmaceuticals for clinical treatment.

The variety of ethnobotanicals obtained from Hawai'ian medicinal plants and comprehensive information on preparation of their extracts can be found in the published works of Drs. Abbott and Shimazu.¹ A list of the more common of these "medicinal plants" is provided in Table 1. Extracts of these plants were, and continue to be, prepared using a variety of methods for use as topical application and/or oral administration, either as a chewable extract or as a liquid often prepared as a fermented or brewed mixture.

One of the better-known Hawai'ian medicinal plants that has been used extensively throughout Polynesia is noni, or *Morinda citrifolia*. Also known as the Indian Mulberry, noni belongs to the *Rubicaceae* family which includes about 450 genera and approximately 5,500 species, found mainly in the tropical areas of Africa, Asia and throughout Polynesia. In Hawai'i, this family of plants is represented by 13 genera, 4 of which are endemic.^{1,4,5}

Hawai'ian *kahuna* have been using extracts of the fruit, leaves and bark of *Morinda citrifolia* to treat a remarkably wide variety of ailments, including urinary disorders, respiratory conditions, diabetes, hypertension, diarrhea and arthritis.³ Noni extracts are now available as non-prescription herbal preparations and recommended for the treatment of clinical conditions as different as cancer and drug addiction.⁶ In the absence of the spiritual component, are extracts of noni any more than a placebo addition to the *kahuna's* art? Does noni have chemicals capable of providing relief or cure such a wide variety of diseases as an over-the-counter medica-

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Table 1. A summary of the most common Hawaiian medicinal plants

Plant name	Hawaiian name	Part(s) used	Medicinal use
<i>Solanum nigrum</i>	Popolo	Leaves, stems, fruit	Respiratory infections, sprains, boils, burns, wounds
<i>Piper methysticum</i>	'Awa	Leaves, bark, roots	Headaches, colds, pulmonary disorders
<i>Aleurites moluccana</i>	Kukui	Flowers, nuts, bark	Laxative, asthma, sores, ulcers, swollen womb
<i>Morinda citrifolia</i>	Noni	Fruit, leaves, bark	Urinary disorders, deep cuts, asthma, diabetes, high blood pressure
<i>Cordyline terminalis</i>	Ki; Ti	Flowers, leaves	Asthma
<i>Artocarpus communis</i>	'Ulu	Sap from tree	Ulcers, cuts, scratches, scaly or cracked skin
<i>Eugenia spp.</i>	'Ohi'a	Leaves, buds, bark, roots	Colds, cuts, sores about the mouth
<i>Scaevola spp.</i>	Naupaka	Bark of roots	Cuts, skin disorders
<i>Bidens spp.</i>	Ko'oko'olau	Flowers	Stimulating appetite, asthma
<i>Saccharum officinarum</i>	Ko	Shoot	Cuts
<i>Coix lacryma-jobi</i>	Pu'ohe'ohe	Leaves	Diabetes
<i>Erythrina sandwicensis</i>	Williwili	Flower	Venereal diseases

This information was compiled from the 1985 publication by Abbott and Shimazu.¹

tion? Is it, as described in lay literature, the "Prize Herb of the South Pacific", the "Molecular Miracle" or the "Wonder Herb" ^{6?}

The composition and biological activity of noni extracts

The most complete study of the composition of noni was published recently by Yoshikawa and co-workers.⁷ These authors reported some of the chemical constituents of the dried root of a Chinese variety of noni, *Morinda officinalis*, as iridoid lactones, together with anthraquinones, iridoid glucosides, a monoterpene glycoside, two sterols, an ursane-type triterpene and a lactone compound. This information augments a previous report describing monotropein and asperuloside acetate as components of the root of this Chinese variety of noni.⁷

Levand and Larson⁸ have identified some chemical components of the dried fruit of the Hawaiian noni. These include acetyl derivatives of asperuloside and glucose. Caproic and caprylic acid were also identified in extracts of dried fruit of *Morinda citrifolia*. These authors were, however, unable to confirm the possible antibacterial action of asperuloside. Similarly, a detailed antimicrobial and anticomplement study of extracts of a large number of Hawaiian medicinal plants, including noni, did not reveal any antimicrobial activity against cultures of *Streptococcus*, *Staphylococcus*, *Pseudomonas* and *Escherichia coli*.⁹ Moreover, no antiviral activity against HIV-1 was noted for both a water-soluble and a dichloromethane extract of noni.¹⁰

In contrast to the lack of confirmed anti-bacterial and anti-viral effects of noni extracts, several reports have demonstrated significant anti-cancer activity. Hiramatsu and co-workers¹¹ have reported that a compound in noni root extracts, damnacanthal, induced a normal, non-tumorigenic phenotype in *ras*-transformed cells. This study indicated that this reversion phenotype was specific to *ras* and induced actin fiber re-organization. These authors also noted that the effect of damnacanthal was reversible, as the tumorigenic phenotype of the *ras*-transformed cells would return once the noni-derived compound was removed from the cultured cells.

In a preliminary report¹², ethanol extracts of noni were found to possibly increase the life span of mice inoculated with Lewis lung carcinoma. These noni extracts moreover were not cytotoxic to human nasopharyngeal carcinoma cells *in vitro*, suggesting that these extracts acted to suppress tumor cell growth through an indirect mechanism. In a subsequent publication, these authors provided evidence suggesting that this mechanism of tumor suppression might be mediated through immuno-modulation.¹³

While there is a report that at least one Polynesian community used extracts of noni for the treatment of breast cancer,¹⁴ there is no published account of the effects of noni on either the biology or clinical progression of breast cancer. In an unpublished observation, however, we have noted a marked growth inhibitory effect of a noni extract on a line of breast cancer cells in culture (Figure 1). An aqueous extract of the noni fruit was observed in these studies to specifically inhibit

the growth of a line of breast cancer cells by up to 80%. This effect was noted in cultured cells and, if confirmed in animal studies, suggests that the mechanism of action of noni on breast tumor growth might be different to the immunosuppression of lung carcinoma suggested by the studies of Hiramizu and colleagues.¹³ This difference in action could either be tumor-specific, or be due to different noni extracts that may have different anti-tumor properties.

A study of the behavioral effects of a noni root extract in mice revealed a significant reduction in locomotor activity, in addition to sedative and analgesic effects.¹⁵ There are also earlier reports of an antihypertensive effect of *Morinda citrifolia*¹⁵ that may be related to these analgesic effects.

Finally, a discussion by R.M. Heinicke in a 1985 article in *The Bulletin of the Pacific Tropical Botanical Garden*,¹⁶ summarizes this author's attempt to identify a component(s) in noni that may be responsible for the many diverse effects attributable to extracts of this plant. The author claims to have identified an unusual alkaloid that he suggests may be the compound that could be responsible for many of the curative properties of noni. There is, however, no documented evidence to support this summary so the significance of these claims is difficult to assess.

In summary, extracts of noni do seem to have some biological effects. While antibacterial effects seem to be inconsistent, noni extracts do have some anti-tumorigenic properties, both in cultured cells and possibly also in limited animal studies. Moreover, a sedative and analgesic effect has been noted in animal studies. No reliable documentation exists however to support the claims that noni extracts are, or could be, active in the wide variety of disorders suggested in the lay press.¹⁷ This is of particular note as the brief and unsubstantiated summary by Heinicke is widely quoted as "evidence" for the role noni extracts play in controlling a variety of biological activities.¹⁷

Nutraceuticals and human health

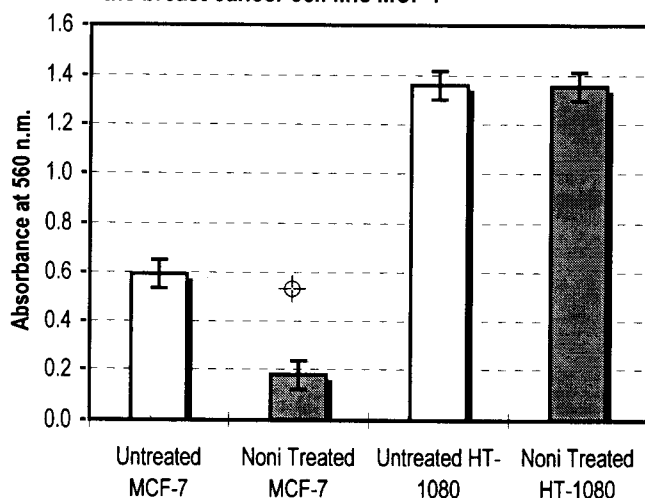
Unsubstantiated health claims in the herbal market are not unique to extracts of noni. There exists very limited and, at times, very controversial evidence in support of the clinical effects of extracts or substances such as Melatonin.¹⁸ There is however increasing evidence in at least a select group of food extracts (nutraceuticals) of a pharmacologic effect in well-controlled animal studies. An excellent example of a thoroughly studied nutraceutical is an ingredient of curry powder called curcumin. Curcumin has been shown in several animal studies and cell based assays to have a pronounced anti-tumorigenic effect, both in colon cancer and skin tumors.^{19,20} This very suggestive evidence that curcumin may have a prophylactic effect in tumor growth has prompted the initiation of some of the first clinical trials of curcumin to document such potential effects in humans.

Clinical trials of several well-known herbal extracts have also been conducted in recent years.²¹ These include the cardiovascular effects of garlic, the anti-depressive effects of St. John's Wort, and the beneficial effects of Ginkgo on a variety of conditions, including several neurological disorders.

A better analysis of Polynesian plant extracts is needed

Almost 2,000 years of ethnomedicine has indicated that a number of Polynesian plant extracts have pharmacologic action. Several limited studies in more recent years have provided at least some support for the use of these ethnobotanicals in treating a variety of human diseases. However, it should be evident from this brief summary of the available literature on one of the more common Polynesian plant extracts, that only a limited amount of information is currently available to support the biological effects and, to date, no evidence is available that demonstrates even a single

Figure 1. Growth regulatory effect of noni extract on the breast cancer cell line MCF-7



Human breast cancer cells (MCF-7) and a human fibrosarcoma cell line (HT-1080; ATCC: CCL 121) were treated with an aqueous extract of the noni fruit for 5 days. Using a commercial kit (an SRB assay from Boehringer Mannheim) for the spectrophotometric measurement of cell proliferation, the growth rate of the breast cancer cell line showed an almost 80% decrease following noni treatment while there was no growth inhibitory effect of the Noni extract on the HT-1080 cells.

⊕ indicates a statistically significant difference to untreated MCF-7 cells ($P < 0.001$).

The results presented were obtained from the average of triplicate cell cultures and the error bars represent standard deviation.

effect of noni in humans. In spite of this lack of scientific evidence, noni is currently receiving a great deal of attention in the currently unregulated herbal market in the United States.²² To realize the considerable potential of ethnobotanicals like noni, it is imperative that efforts in understanding the biology and pathobiology of these ethnobotanicals be continued, both in animal studies and in human clinical trials. Thorough analysis of the biological effects of Polynesian plant extracts will be the only way in which the full potential of these extracts can be examined out of the confines of traditional ethnomedicine. It is also the only mechanism through which island communities such as Hawai'i can fully explore the very significant potential these indigenous plants have in new drug discovery.

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