

From Polynesian Healers to Health Food Stores: Changing Perspectives of *Morinda citrifolia* (Rubiaceae)

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Morinda citrifolia L (noni) is one of the most important traditional Polynesian medicinal plants. Remedies from isolated Polynesian cultures, such as that of Rotuma, illustrate traditional indications that focus upon leaves, roots, bark, and green fruit, primarily for topical ailments. Anecdotally collected Hawaiian remedies that employ noni fruit illustrate changing usage patterns with shifts in recent times to preparation of juice made of ripe or decaying fruit. Ralph M. Heinicke promoted a wide range of claims about noni, and these seem to have fueled much of the current commercial interest in the plant. Recent studies of the proliferation of commercial products have shown that noni product manufacturers are promoting a range of therapeutic claims. These claims are based upon traditional Polynesian uses, Heinicke's ideas, and fragments of recent scientific studies including the activity of noni in the treatment of cancer. A review is provided of recent studies of potential anticancer activity of noni fruit. While noni's anticancer potential is still being explored, it continues to be widely used by Polynesians and non-Polynesians alike for both traditional and newly hypothesized indications.

Over the last 20 years, a few plants that have been used in traditional Polynesian medicine have become quite popular in North America and Europe. Two among these, kava (*Piper methysticum* Forster f, Piperaceae) and noni (*Morinda citrifolia* L, Rubiaceae) stand out as claiming major market shares and being uniquely introduced from the Pacific Islands. A rapid review of the literature on medicinal plants of the Pacific seems to support the status of these 2 and to also promote a range of other medicinal plants. Table 1 includes more commonly reported medicinal plants of Polynesia with hypotheses of indications based upon traditions of usage. Although modern uses of kava can be easily correlated with some of the ancient uses, the same cannot be said for noni. The primary purpose of this paper is to explore the apparent disjunct between the traditional uses of noni and the modern claims promoted by producers and marketers of products.

Morinda citrifolia is a bush to small tree (Figure 1) growing from 2 to 6 meters tall. Distinctive varieties

exist with differing leaf morphology. Leaves may be rounded, elliptic, or long and strap-like. Larger rounded leaves are 15 to 30 cm wide by 20 to 40 cm long. Strap-like leaves may be as narrow as 10 cm, and as long as 60 cm. The globular compound fruits vary in size from 3 to 10 cm wide and are sometimes over 20 cm long. Fruits are green until maturity, when they rapidly change to a light yellow, then light yellow and translucent white (Figure 2). Fruit scent varies, with some varieties being virtually odorless, but more common, vigorous growing varieties having a strong smell of butyric acid when ripe. The roots and inner bark may have little coloration or may range from bright yellow to red. I have found the trees growing in sandy soil on very isolated, dry atolls as well as in rich volcanic soil at higher altitudes on wet islands.

M. citrifolia is commonly assumed to have originated in Southeast Asia⁸ and subsequently distributed by humans or other means into the islands of the western Pacific. Guppy⁹ determined that *M. citrifolia* seeds could be distributed by floating in the ocean and probably secondarily by birds and other animals. His work supports the notion that the plants could have distributed themselves naturally throughout the Pacific islands. Phylogenetic research in New Caledonia has demonstrated that *M. citrifolia* is nested within a clade of Southwest Pacific endemic species, making it possible that it originated there rather than in Southeast Asia¹⁰. Whistler,¹¹ Abbott,¹ and others believe that the plant was intentionally distributed as a medicinal plant by the ancient voyagers who colonized the Pacific Islands. They believe the plant to be naturally distributed throughout the western Pacific and human-distributed in the Eastern Pacific islands including Tahiti and Hawai'i. Whether it was distributed by people or nature does not matter since in either case, it is likely that Pacific Islanders have had

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From Polynesian Healers to Health Food Stores

Table 1. Some Important Pacific Island Medicinal Plants and Likely Indications Based Upon Traditional Usage*

<i>Species</i>	<i>Probable Indication(s)</i>
<i>Aleurites moluccana</i> (L) Willd (Euphorbiaceae)	Seeds/oil: laxative/purgative, infection. Bark: asthma. Flowers/Fruit/Sap: infection(fungal). Leaves: inflammatory.
<i>Calophyllum inophyllum</i> L (Clusiaceae)	Leaves: ocular irritation, infection (bacterial/fungal), inflammation. Fruit: seborrhea, topical irritation.
<i>Centella asiatica</i> (L) Urban (Apiaceae)	Leaves: thoracic pain, infection(viral), fever.
<i>Cordyline fruticosa</i> (L) A Chev (Dracaenaceae)	Young Leaves: asthma. Leaves: fever/headache/inflammation.
<i>Curcuma longa</i> L (Zingiberaceae)	Rhizomes: infection(bacterial/fungal), constipation.
<i>Morinda citrifolia</i> L (Rubiaceae)	Roots/Bark: infection(bacterial), termination of pregnancy. Green Fruit: halitosis, infection (bacterial/fungal), menstrual cramps, arthritis, gastric and oral ulcers, toothache indigestion. Ripe Fruit: infection (bacterial/helminthic), promotion of lactation, purgative. Leaves: infection (bacterial), inflammation.
<i>Piper methysticum</i> Forst f (Piperaceae)	Leaves: restlessness, menstrual irregularities, inflammation, insect stings. Root/Rhizome: headache, inflammation, muscle soreness, tranquilizer, difficulty in urination, menstrual irregularities, bronchitis/respiratory tract congestion, displacement of the womb.
<i>Premna serratifolia</i> L (Lamiaceae)	Leaves: cough, constipation. Bark: hypertension, cardiac insufficiency.
<i>Solanum nigrum</i> L (Solanaceae)	Leaves/Fruit: infection (bacterial), improved digestion, respiratory tract disorders.
<i>Syzygium malaccensis</i> (L) Merr & Perry (Myrtaceae)	Bark/Leaves: sore throat/bronchitis, venereal disease, infection (bacterial).
<i>Tarenna sambucina</i> (Forst f) Durand (Rubiaceae)	Bark: inflammation/fever, diarrhea, stomachache. Leaves: inflammation.
<i>Thespesia populnea</i> (L) Soland ex Correa (Malvaceae)	Bark: cough, asthma, diarrhea, infection (fungal/viral), fever, seizures. Fruit: infection (bacterial/viral/fungal), headache, inflammation.
<i>Zingiber zerumbet</i> (L) Sm (Zingiberaceae)	Rhizomes: diabetes, cough, infection (viral?), stomachache, inflammation. Burned Leaves: infection (bacterial).

*See references 1-7.

access to and experience using *M citrifolia* for thousands of years.

Morton⁸ has reviewed the economic uses of various parts of *M citrifolia* including the use of fruits and leaves for food and medicine. The references cited by Morton are mostly those written by botanists as part of floral treatments and not those of social scientists or nutrition scientists with direct observations of human activities. Terra¹² reported some nutritional characteristics of the leaves and fruit, noting good levels of ascorbic acid (24-258 mg/100 g dried fruit). Within the Pacific Islands, a major compilation of information on food¹³ does not include *M citrifolia* because it is of so little consequence in modern diets. Based upon my conversations with traditional cultural experts from Fiji, Hawai'i, Rotuma, Samoa, Tahiti, and Tonga, it seems unlikely that the plant ever played a significant role in ancient diets. However, Lucas¹⁴ interpreted elements of the following ancient Hawaiian chant (recorded in 1861 about the interactions between the

gods Kamapua'a and Pele) as evidence that noni fruit was once eaten in times of famine.

Kamapua'a chanted as follows:

"I have come now from Puna.
I have seen the women gathering noni,
Scratching noni,
Pounding noni,
Marking with noni."¹⁵

Noni bark or roots are employed in Hawai'i and elsewhere as a dye used on *Broussonetia papyrifera* Vent (Moraceae), felted clothing (so-called "bark cloth"). The inner bark of *M citrifolia* is scraped or "scratched" off of the tree and pounded in the dye production process. The final dye is then painted (or marked) on the clothing. The passage of the legend can be interpreted as referring to the process of preparing this dye and may have nothing to do with consumption of the fruit. *M citrifolia* bark (and other parts) contain a



Figure 1 *Morinda citrifolia* tree in Hawai'i.

number of anthraquinones that are responsible for traditional use of the root and stem bark as a dye¹⁶. Morton⁸ speculated that the anthraquinones are the reason that bark extracts are used to treat ringworm.

Morton⁸ refers to a scarcity of the plants in Hawai'i and references Degener,¹⁷ who felt that the plant had become less abundant. Currently, noni is not uncommon throughout Hawai'i, particularly in dryer areas such as near roads/houses, on young lava flows, and in house yards in dryer leeward parts of each island. On Kaua'i, several valleys have abundant stands that are harvested for commercial purposes. Locations on O'ahu, Maui, and Hawai'i now have commercial plantations from which fresh and dried materials are prepared.

***Morinda citrifolia* in Traditional Medicine of Polynesian Cultures**

M. citrifolia is arguably the most important medicinal in Polynesia, based upon the number of indications reported and the breadth of usage across cultures.^{7,18,19} Among the elderly healers whom I have interviewed in Hawai'i, Samoa, Rotuma, and Fiji, almost all have discussed use of this plant. The most commonly used part is the leaf. Varieties with strap-like leaves are held briefly over a fire and then placed over wounds as a

bandage. (When leaves are heated and wrapped around an appendage, the overlapping leaf will stick to itself.) Macerated or chopped leaves are also commonly placed within wounds. Young, green fruits are the second most commonly used part. These are used primarily in external remedies but sometimes are used in treatments of diseases afflicting the inside of the mouth. Root bark and inner stem bark are the next most commonly used parts. Each of these are used in externally apparent inflammatory or infectious processes. Ripe fruits are not commonly used by expert healers; however, they are widely used by nonhealers in home remedies for external wounds and infections. For instance, crushed fruits or slices of fruit may be placed on foot, leg or arm infections. The logic that is typically expressed for this use is that the fruit is thought to "draw out" the source of the problem. This is not unlike the ancient European concept of a drawing salve.

Among the Pacific island communities in which I have worked, those on the Polynesian island of Rotuma (north of Fiji) were the most isolated and "traditional". At the time of my field work (1990-1993), the economy of Rotuma was still largely subsistence-based and traditional medicine served as the primary health care system. In 1991, a survey of the population was conducted,¹⁸ identifying 69 women and men recognized as having specialized skills and training, eg, healers. Each of the healers were then interviewed about plants and other aspects of their traditions. *M. citrifolia* (known as 'ura on Rotuma) was the most widely reported ingredient in herbal remedies, often being used in conjunction with other species. Examples of remedies employing *M. citrifolia* are listed in Table 2.

During one 4-month period, I lived in a thatched house with a 'ura (noni) tree adjacent to the entry doorway. The tree produced a modest amount of fruit that never had an unpleasant smell. Healers with whom I was working identified that particular tree as having specific medicinal uses that differed from the uses assigned to 2 other "varieties" that they recognized. At least according to the healers of Rotuman traditions, there is more than 1 species nestled within the current circumscription of *M. citrifolia*. Three varieties (or species) recognized by Rotuman healers are: (1) trees with small elliptic leaves having many small fruit arranged at nodes along the branches, and thin stems/branches whose bark and roots are used for dyes, (2) trees with long, strap-like leaves, having larger, lightly scented to nonscented fruit, thicker stems and shorter branches that are used for most medicinal purposes (Table 2), and (3) shorter bushy trees with large elliptic to round leaves and large, strong smelling fruit that are not commonly used



Figure 2 *Morinda citrifolia* fruit: young green fruit with flowers, green fruit, and mature white fruit.

medicinally, although the ripe fruit is used in externally applied home remedies (remedies used by nonhealers).

Rotuman treatments that employ *M. citrifolia* are mostly topical, involving immature fruits or mature leaves. Rotuman healers using these remedies ranged in age from 21 to 80 years old. Younger and older healers both used *M. citrifolia*; however older healers knew more kinds of remedies. While I was on Rotuma, there was no commercial trade in medicinal plants and no real influence from outside of the culture driving them to use plants in other than traditional ways. Younger healers tended to know less, probably due to lack of experience and training rather than loss of cultural knowledge. Younger healers were being trained by their elders throughout their lives. Elder healers knew about each other and their individual specialty areas. Patients were regularly referred from one healer to another when it was thought that certain kinds of expertise were needed. Thus, the system of health care in this small culture of only about 2500 local residents on 1 island, was unified as a single health care delivery system.

The situation is quite different in the much larger Hawaiian culture that is spread across 7 major islands with a population of over 300,000 now and probably well over 1 million in pre-European contact times. Commercial trade in medicinal plants is common in Hawai'i, particularly in non-Hawaiian communities. Although there are prominent healers know who each other, there does not seem to be a strong cohesion, particularly between islands and between knowledge

lineages. Generally, elderly healers carry on traditional practices with traditional beliefs about health and wellness. Younger healers may also follow traditional practices or may have become involved in commercialization of the traditional health care system. The dichotomy between traditional healers and non-traditional healers is growing, particularly in 2 areas: incorporation of nontraditional explanations for disease and treatment, and charging for services and medications.

When asked about use of *M. citrifolia*, elderly Hawaiian healers spoke of it as being a powerful plant that is usually too strong to use. Among 6 elderly healers I interviewed about noni fruit, each indicated that they knew of its use by other Hawaiians but had not learned to use the fruit in their own particular tradition. Each healer did use the leaves in various remedies and 1 used young fruit for mouth sores. None of the healers over the age of 50 discussed using fermented fruit (as described below) and only rarely was the fruit described as being medicinal. When the fruit was used in internal remedies, it was usually the younger, green fruit and not the mature fruit. However, 1 of the more commonly reported uses of *M. citrifolia* is external application of crushed or sliced mature fruit to skin lesions and wounds. These uses are consistent with the first 2 in Table 3 as reported from the literature. One of the students of an elderly healer (Mr Russell Ili), who is attempting to closely follow the traditional remedies, told me that he has also used ripe fruit prepared as a poultice for treatment of skin infections but that he was not taught to use the fruit internally by his

Table 2. Traditional Rotuman Treatments Employing *Morinda citrifolia* ('ura)

<i>Disease state</i>	<i>Treatment</i>
Sores or scabs around the mouth, whether associated with mamosa (lethargy, weight loss, dry cracked tongue, and loss of appetite), or alone (nuj ko') but which are persistent:	Immature (green) fruits are crushed and the juice extracted. This juice is added to the fresh yellow film removed from the seeds of the pinau, <i>Thespesia populnea</i> (L) Corr Serr, and the mixture is applied to the external sores. The treatment will not only alleviate the lesions but will also relieve pain associated with the lesions. The 'ura fruits may be used alone to treat the sores, in which case the crushed fruits are placed in an ununu (coconut petiole fiber mesh, functionally like cheese cloth) and squeezed until juice is freely leaching from the ununu. The ununu is then daubed on the lesions as needed to apply the juice.
Nuj ko' (sores found within the mouth):	Immature fruits are crushed and mixed with coconut oil. The mixture is placed in an ununu, then wrapped with a banana leaf and heated over a fire. After heating, the ununu is squeezed, and the resulting warm solution is drunk. In children, only a small dose can be given because higher doses will cause nausea and vomiting. Occasionally this is given in the higher dosage to promote vomiting and thus remove the cause of the illness. This is usually the case if the illness is felt to reside in the throat and/or if there is mucus built up in the throat.
Susun (topical burns)	Leaves are applied to the site of the burn until wilted and then are replaced with fresh leaves. The treatment is repeated until the leaves no longer wither and the fever discontinues.
Filo'u (headaches) and fever	Leaves are applied and the head massaged with the leaves until the leaves are wilted. The treatment is repeated until the leaves no longer wither, and the fever and headache discontinue.
Neonatal inability to breath immediately after birth	Upon delivery of a child that is not breathing, the midwife will wrap the umbilical cord with a pair of 'ura leaves to promote breathing. If breathing does not occur then, the midwife will begin to pile 'ura leaves on the child until it begins to breathe.
Promotion of good postparturition health of the mother	A midwife boils 'ura leaves in coconut oil; they are then mixed with mena (dried, powdered <i>Curcuma longa</i> L rhizomes) and rubbed over the entire body of the new mother.
Koi mosran (stonefish spine poisoning)	Upon presentation of a patient who has been penetrated by the poisonous spine of a stonefish, the healer will dig up and clean an 'ura root. Once cleaned, the outer bark will be scraped off and placed in an ununu or piece of cloth. The area of the wound will be slightly enlarged with a knife to allow a free flow of blood. Once blood is flowing, a leaf of the majila, <i>Chamaesyce atoto</i> (Forst f) Croizat, will be broken off, and the pul (milky latex) dabbed on the site. Following a thorough application of the pul, the ununu will be held over the wound and squeezed to release a few drops of juice into the wound. More of the pul may be applied if the wound continues to bleed. The stonefish toxin produces a great deal of pain and inflammation. The pain will dissipate within 5 minutes of application. The inflammation will recede in the following several hours with a proportional time frame depending on the lapse between the time of injury and that of treatment. Any majila or 'ura root material that remains must be discarded in the ocean. No further treatments are needed, and no restrictions or recommendations are made to the patient. Another remedy for the same ailment involves the following: Young 'ura leaves are pounded together with entire cleaned usogo plants, <i>Laportea interrupta</i> (L) Chew. The mixture is placed in a piece of thin cloth and a small amount of coconut oil is added. The cloth is then wrapped with 2 'ura leaves and placed over a fire to be heated. The site of the poison puncture is enlarged with a knife. The hot package is removed from the fire, and small amounts of the juice dripped into the wound. The juice is only applied to the site, and care is taken to ensure that it does not get anywhere else on the individual. Massage will next be conducted using a small amount of the juice on the adjacent skin. The massage is always in the direction of the injury. From the beginning of the preparation until the treatment has been completed and the pain relieved, usually requires about 1 hour.
Hiaj ne to' (bone fractures or dislocations)	'ura leaves will be wrapped over the skin and tied on after the bone has been set but before the splints have been applied.

Table 2. Continued

Disease state	Treatment
Bleeding caused by a bone puncture	If, after setting a broken bone, persistent bleeding from the site of bone penetration occurs, then the bonesetter will crush several sesei, <i>Phymatosorus scolopendrium</i> (Burm) Pichi-Serm, leaves in some water. The leaves will be discarded and the solution applied to and washed over the cut. After thorough cleaning, 2 fresh 'ura leaves will be rolled between the hands to release a thick green juice, which is placed on the cut to stop the bleeding.
Li ne uaf (a badly infected cut)	A solution will be prepared as above (for bone punctures), and the infected area washed thoroughly. An 'ura root is cleaned, and the bark scrapped off into an ununu. The ununu is held over the infection and squeezed to release juice on the wound. The wound will begin to bubble and it is felt that the infection is now being forced out of the cut. No restrictions are placed on the treated individual, and the treatment is not repeated.
Mea ta koi (a skin disease possibly fungal that starts as a red spot on the skin and spreads as a ring, then rapidly spreads over the whole body; said to lead to death if untreated)	Two very young coconut, <i>Cocos nucifera</i> L, fruits are pounded into a fine paste and added to some coconut oil and a sprinkle of mena <i>Curcuma longa</i> L powder. The mixture is placed in an ununu, which is then wrapped by 2 'ura leaves and placed over a fire. Once hot, the 'ura leaves are removed, and the ununu is placed over the affected area and squeezed to release hot fluids onto the site. Treatment is repeated daily for up to 5 days. No bathing is allowed during the treatment and the affected area must not get wet.
Peeling or cracking of the toes and feet that is not associated with tinea pedis	Ripe fruits are crushed and applied to the affected site. This is not a specialized treatment and requires no specialized application.

Based upon McClatchey (1993)¹⁸.

instructor. Because Hawai'i is a set of islands with many different cultural lineages, there are also different medicinal knowledge lineages. Although the literature and my own limited interviews do not support an ancient Hawaiian tradition of using decaying noni fruit as a remedy, it is possible that such a tradition exists and has simply not been documented.

An issue that seems to be related to the ways in which the fruit is used is reimbursement of healers for treatments and remedies. Both Rotuman and Hawaiian healers who were interviewed expressed concern about the sale of medicines. They generally see medicine as being a gift that should not be bought or sold. They describe themselves as being conduits of healing power and insight that is not their own but a gift from their ancestors or God that passes through them for the benefit the patients. Some Rotuman healers felt that if someone charged for their services or plant remedies, they would lose the spiritual power to heal and might even subsequently contract the disease they were attempting to treat. However, both cultures traditionally recognize the contributions of healers through the giving of gifts from patient to healer, sometimes based upon success of the remedy. Although there are standardized gifts, healers do not expect to receive compensation and are quite understanding when patients are unable to provide a gift of thanks. Rotuman healers specifically shunned gifts of

cash; however some elderly Hawaiian healers who refuse to accept payment for their services, do accept gifts of cash.

Hawaiian healers live in a modern, cash economy with all of the stresses and pressures that accompany the benefits of such societies. It is not surprising that some are modifying traditional practices to earn a living as health care providers. It would not surprise me to see similar changes happen in the Rotuman community as they become more integrated into cash economies.

No scientifically reproducible, ethnobotanical studies have yet been published on Hawaiian traditional medicine; however, many books have been published about Hawaiian remedies. Table 3 provides a selection of these remedies. It is unclear from the sources if information was gathered from professional healers or merely those with knowledge of home remedies. The first 3 disease states listed include treatments that are consistent with traditional practices elsewhere in Polynesia and are therefore probably of ancient origin. The next 3 remedies are uniquely Hawaiian and difficult to compare to other Pacific cultures. The last 2 remedies are surely of modern origin, since 1 is for the treatment of a recently introduced disease, tuberculosis, while the other is a generalized tonic for diseases that are probably only recognized recently in Hawaiian communities.

Table 3. Some Traditional Hawaiian Treatments* Employing *Morinda citrifolia* Fruit

<i>Disease State</i>	<i>Treatment</i>
Poultice	Green or ripe fruit used as a poultice on wounds, boils, or pimples. Some applications involve the addition of salt to the poultice or heating of the fruit before it is applied. ^{3,17,20}
Promotion of lactation	Tender (young?) leaves were heated over a fire and placed on the mother's breast while prayers to Ku and Hina were chanted. ³
Purgative	Pounded young noni (fruit?) strained and mixed with sugarcane juice and mashed kukui (<i>Aleurites moluccana</i> (L) Willd, Euphorbiaceae) nut were consumed orally. ³ Another remedy used ripe fruit macerated and strained with koali (<i>Ipomoea cf indica</i>) roots, 'ilima (<i>Sida fallax</i> Wallp, Malvaceae) roots and bark, puakala (<i>Argemone glauca</i>) leaf bud, ko maulele (<i>Saccharum officinarum</i> L, Poaceae) juice, cooked egg yolk, and starch. ²⁰
Blood purification	Fruit combined with cooked niu (<i>Cocos nucifera</i> L, Arecaceae) and ko manulele (<i>Saccharum officinarum</i>) are combined with water and drunk. ²¹
Counteracting unpleasant side effects of 'awa intoxication	Fresh spring water and the juice of noni fruit were mixed into a drink called aumiki 'awa. This could then be consumed by those drinking 'awa (<i>Piper methysticum</i> Forst f, Piperaceae). ¹⁷
Insecticide	Fruit juice was used to wash hair. ¹⁷
Akepau (tuberculosis)	Noni fruit, ko' 'ele'ele (<i>Saccharum officinarum</i>) stem, and 'awa (<i>Piper methysticum</i>) root were each pounded and strained separately and then mixed. A little koae (red clay) was then added and the liquid was brought to a boil by addition of hot stones. Once hot, the liquid, called aumiki 'awa or apu 'awa was drunk. ¹⁶ A similar remedy is reported later by Chun. ²¹
Diabetes, heart trouble, and high blood pressure	Juice was diluted with water and used as a drink before meals and resting periods. ²²

*Extensive lists of medicinal uses for *M citrifolia* are reported in references 23 and 24.

***Morinda citrifolia* in Commercialized Hawaiian Medicine**

Much of the interest in commercial production of noni products can be traced to an outrageous publication in the Pacific Tropical Botanical Garden Bulletin.²⁵ This unreferenced and authoritatively written report appearing in an horticultural bulletin, proposes the presence of an active compound in *M citrifolia* known as xeronine, which is said to be derived from a precursor, proxeronine. It is interesting that this seemingly biochemical report is published in the bulletin of a botanical garden, because it may have been better published in the Journal of Irreproducible Results. No chemical structure is given for the "alkaloid" xeronine, although many results are discussed without a clear indication of the scientific research from which they are derived. Among the results are the following that continue to impact marketing and consumption of noni products.

1. The enzyme bromelain has an unknown ingredient responsible for its clinical activity: namely a "relatively

small alkaloid that is physiologically active in the picogram range": xeronine.

2. Xeronine is derived from a "strange" colloidal molecule known as proxeronine that is relatively large (molecular weight about 16,000). Proxeronine contains neither sugars, amino acids, nor nucleic acids.
3. Noni juice is pharmacologically inactive unless taken on an empty stomach because a proenzyme that is susceptible to pepsin and acid in the stomach is needed to convert proxeronine into xeronine.
4. Each body tissue has cells that contain proteins that have receptor sites for the adsorption of xeronine. These protein receptors are responsible for the efficacy of a wide range of bioactive plant products.
5. Noni is less effective when taken with coffee, tobacco, or alcohol, and concomitant use of these with noni may result in "some unexpected side effects."
6. Green fruit has more potentially valuable components and less undesirable flavor than ripe fruit.
7. Potential indications are: "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."

I have not located any subsequent publications reporting a structure for xeronine or proxeronine, although much chemical work has been conducted. If this question has not been resolved, then much of Heinicke's report should be in question. If, on the other hand, xeronine is described, then this may lend support to his other findings and open the door for production of specific commercial products.

Many modern, commercialized healers in Hawai'i claim that noni has miraculous powers, particularly in the treatment of diabetes and cancer. Dixon et al²⁴ have summarized the claims (Table 4) of commercial producers of noni products. Younger healers are in some cases associated with companies, as either the sources of plant materials/products or as advocates of a particular product line. Contrary to the perspectives of traditional healers, the commercialized healers are willing to charge for their services and products, and they see the powerful nature of noni as something to be used within their practices.

Typical modern usage of noni in Hawai'i involves the following process. First, fully ripened fruits are cleaned and placed in a glass jar. Usually the jar is filled with fruit although not packed tightly. Fresh, cool, water (sometimes spring water) is placed in the jar until all fruit are covered. A lid is tightly sealed on the jar, and the contents allowed to decompose. Some individuals keep the jar in a refrigerator while others prefer to keep it at room temperature or even store it in sunlight.²⁴ After a few days, the liquid in the jar may be decanted and consumed. Commonly, a tablespoon to a cup of the liquid will be consumed at least once per day. As the fluid volume decreases from usage, more water may be added to the jar of fruit.

Although decomposed noni fruit is consumed as a liquid in modern Hawai'i, an array of other forms have been developed for easier marketing, greater consistency of dosage and product, and presumably, longer shelf life. These include preserved juice drinks, encapsulated freeze-dried fruit juice, concentrated extracts, powders, tinctures, and even fruit leather. Many of these products are made with ripe or subripe fruit that is processed without decaying or adding water. The fruit may be chipped and dried (Figure 3) in commercial farming operations for later rehydration and juice extraction in distant factories.

Isabella Abbott (personal communication) has proposed that the use of noni in a decomposed form is based upon a Chinese-introduced technology. Indeed, prior to the arrival of Europeans in the late 1700s, Hawaiians had no sealable glass or other containers. Dixon et al²⁴ have likewise stated that the mode of preparation is consistent with Chinese technologies for food preparation that are prominent in Hawai'i's

Table 4. Selected Claims for Modern Noni Products

Claims apparently based upon Polynesian traditional uses

1. Inflammation (possibly extended to lupus)
2. Headache
3. Fever
4. Arthritis
5. Sore gums, gingivitis, toothache, abscess
6. Respiratory disorders
7. Sore throat with cough
8. Infections (bacterial/fungal/viral/helminthic)
9. Tuberculosis*
10. Diarrhea
11. Gastric ulcer
12. Indigestion
13. Diabetes*
14. High blood pressure*
15. Dermatological effects†
16. Childbirth†
17. Menstrual cramps

Claims apparently based upon Heinicke²⁵

1. Xeronine and proxeronine are active ingredients.
2. Production of xeronine is promoted by noni juice.
3. Xeronine can regenerate cells, cause cellular repair, (anti-aging).
4. Mental depression
5. Atherosclerosis, blood vessel problems
6. Drug addiction
7. Senility
8. Analgesia

Claims presumably of more recent origin

1. Immune system stimulant
2. Menstrual cycle regulation/pregnancy‡
3. AIDS
4. Prevents activation of Epstein-Barr virus.
5. Antitumor/anticancer activity, specifically, breast cancer
6. Internal disorders‡
7. Kidney problems‡
8. Lupus
9. Blood purifier/cleanser‡
10. Weight loss
11. Cleansing‡
12. Nervous system‡

Note: See reference 24 for modern noni products.

*Disease state that may not have been recognized in ancient Polynesia, but for which "traditional" remedies have recently been recorded.

†Vague claim probably based upon one or more traditional uses.

‡Vague claim.

ethnic Chinese communities. In ancient times, the same process could probably have taken place (at least in part) in an open wooden or gourd bowl, but I could find no evidence of such practices. The oldest Hawaiian record that is reminiscent of the modern production process comes from Degener¹⁷ who reports that fresh spring water was mixed with juice of the fruit to produce a drink used to treat side effects of 'awa (*Piper methysticum*) intoxication.

The popularity of *M. citrifolia* fruit in modern Hawai'i seems to hinge on a combination of its tradition of use among Polynesians, development and



Figure 3 Chipped and dried *Morinda citrifolia* fruit and *Piper methysticum* rhizomes prepared on Hawai'i island for shipment to an herbal products manufacturer.

distribution of modern products, and a mixture of factual and fanciful information provided directly by manufacturers and indirectly by academic researchers. Since traditional Polynesian medicines were neither mass produced nor sold, some modifications have been made, including changes in dosage form, standardization of dose, and actual sale of medicine for a profit.

Commercial claims for *M. citrifolia* fruit products (Table 4) have been separated into 3 categories. The first category consists of claims that are probably based upon traditional Polynesian uses and therefore are possibly consistent with ancient ethnopharmacological thinking. The second category consists of claims that are based upon Heinicke.²⁵ Since these claims do not seem to have any prior reference in records of Polynesian traditions, I assume that these are the results of Heinicke's work. The third category includes miscellaneous claims that are either too vague to hold serious meaning, eg being used for "internal disorders", or are likely based upon more recent research in immunology, virology, cancer, and so on.

Cancer Studies With *Morinda citrifolia*

Papa Kalua Kaiahua, a contemporary Hawaiian healing expert stated, "I have used noni to help people with cancer, kidney problems, diabetes, and tumors. . . .

To me, noni is the most important of the herbs used in medicine."²³ Based upon this statement, Hirazumi studied anticancer and immunotherapy potential of *M. citrifolia* fruit for her dissertation project. Hirazumi et al²⁶ and Hirazumi²³ demonstrated that *M. citrifolia* fruit juice is active in the Lewis Lung peritoneal carcinomatosis model²⁷. She determined that juice was able to stimulate an immune response from murine effector cells through the release of several mediators including tumor necrosis factor- α (TNF), interleukin-1 β , interleukin-10, interleukin-12, interferon- γ , and nitric oxide. Hirazumi²³ and Hirazumi et al^{26,28} identified the immunomodulatory activity as occurring in a polysaccharide-rich portion of the juice (aqueous extract). Although the studies of Hirazumi²³ used the Lewis Lung carcinoma model that has been dropped by the US National Cancer Institute, her work has pointed to possible roles of *M. citrifolia* fruit aqueous polysaccharides in mediation of certain kinds of cancer. Wang et al³⁰ isolated a trisaccharide fatty acid ester and 3 novel glycosides³¹ from *M. citrifolia* fruit. Liu et al³² studied 2 *M. citrifolia* fruit glycosides in the mouse epidermal JB6 cell line. They found that the compounds were effective in suppressing TPA- and EGF- induced cell transformation and associated AP-1 activities. Fong et al³³ reported preliminary results of their studies of 4 noni fruit extracts (hexane, ethyl acetate, butanol, and water). Anti-proliferative activity was

identified from the water and butanol fractions against a breast carcinoma cell line (MCF-7) and a colon carcinoma line (HCT-116). Furthermore, they isolated a novel glycoside demonstrating anti-proliferative activity against MCF-7 as well as 6 other active compounds from the butanol fraction. Morphological changes in the MCF-7 cells were reported to be indicative of apoptosis. Finally, they explored the genetic basis for possible apoptosis: "An Atlas cDNA array specific to apoptosis revealed that the active compounds in the water extract appear to affect several genes of the TNF apoptotic pathway and cell cycle, and result in inhibition of cancer cell growth."³³

The National Institutes of Health recently provided support for a phase I clinical study of *M citrifolia* fruit. The principal investigator, Brian Issell, MD, with the Cancer Research Center of Hawai'i, is studying the effects of freeze-dried noni fruit extract in cancer patients. The hypothesis being tested is that noni, at a specific dosing, provides cancer patients with a sufficient benefit-to-toxicity profile to be useful as a therapeutic. The specific aims of the study³⁴ are to:

1. Determine the maximum tolerated dose of capsules containing 500 mg of freeze-dried noni fruit extract.
2. Define toxicities associated with the ingestion of noni.
3. Collect preliminary information on the efficacy of noni in respect to antitumor and symptom control properties to help select specific patients for subsequent Phase II studies.
4. Identify chemical constituents of the extract that can be used to characterize the bioavailability and pharmacokinetics of noni food supplement.

The eligibility criteria for the study³⁴ are:

1. Patients must have a pathologically or cytologically verified diagnosis of cancer and evidence of disease for which no standard treatment is available.
2. Patients must be ambulatory, capable of self care, and up and about more than 50% of waking hours (Zubrod Performance Status 0-2).
3. Patients should have completed all other cancer treatments at least 4 weeks previously.
4. If patients are taking medications that are considered by their allopathic practitioner to be essential for their health (eg antidiabetic, antihypertensive, lipid lowering), they must have been on these medications at consistent dosing for at least 4 weeks prior to starting noni.
5. Patients must agree to take no other CAM **DEFINE CAM** treatments while taking noni and agree to keep a diary, recording all medications taken daily, including all nonprescription products and to record the time that noni is taken.

Conclusions

Ancient Polynesians used *M citrifolia* as one of their primary medicinal plants. As Polynesian traditions have been blended with introduced cash economies, particularly in the heavily colonized islands of Hawai'i, modified medicinal systems have evolved. These systems are based upon both commercialized healers and commercialized plant-based remedies. Elements that have contributed to the commercialization of *M citrifolia* include key publications such as Heinicke,²⁵ technological introductions from other cultures (China?), and shifts from indications with existing over-the-counter commercial products (eg, topical antibiotics) to indications with few satisfactory over-the-counter commercial products (eg, internal treatment of cancer, diabetes, hypertension, etc). As with other panaceas, *M citrifolia* is being marketed as "hope in a bottle," which will "naturally" treat illnesses that are otherwise out of the control of the average person.

In modern society, which is dominated by a bioscience paradigm, claims of efficacy need to be linked to specific chemical causes and mechanisms of action. Heinicke²⁵ provided both of these elements in one fell swoop. Without these supporting "scientific" findings, *M citrifolia* fruit products would probably not have developed as rapidly as they have. It is interesting that although the rationale for turning to natural products is to avoid perceived harshness, reductionist, and "unnatural" attributes of synthetic medicinal products, people still have a desire to know why a natural product works and expect that rationale to include a bioscience explanation of activity.

Claims of efficacy are bolstered by beliefs that the plant being used has been developed by traditional healers. Modern claims for *M citrifolia* are difficult to support in light of actual usage in traditional cultures such as that of Rotuma. Marketing strategies, as reviewed by Dixon et al² follow a bait-and-switch approach, leading with claims that the plant is used by Polynesians, followed by claims that are inconsistent with traditional usage patterns.

Finally, intensive cultural use of a plant, either within other cultures or within Western culture, drives researchers to explore for potential biological activity. This research may initially follow the implied indications of the culture that developed the plant's use. Other leads may be followed as they arise from happenstance of the research process. Although there do not seem to be traditional indications for its use in cancer, *M citrifolia* is offering promise in this area. It seems ironic that the initial drive to explore the fruit for anticancer activity was propelled by the, as yet, unsupported claims of Heinicke.

References

1. Abbott IA. *La'au Hawai'i: Traditional Hawaiian Uses of Plants*. Honolulu, Hawaii: Bishop Museum Press; 1992.
2. Biggs BG. Contemporary healing practices in east Futuna. In: Parsons CDF ed. *Healing Practices in the South Pacific*. Laie, Hawaii: Institute for Polynesian Studies; 1985:108-128.
3. Gutmanis J. *Kahuna La'au Lapa'au: The Practice of Hawaiian Herbal Medicine*. Hong Kong: Island Heritage Publishing; 1994.
4. Krauss B H. *Native Plants Used as Medicine in Hawaii*. 2nd ed. Honolulu, Hawaii: Lyon Arboretum; 1981.
5. McClatchey W. The ethnopharmacopoeia of Rotuma. *J. Ethnopharm.* 1996;50:147-156.
6. O'Rourke-George L. *An Ethnobotanical Study of Traditional Medicine in Tonga* [master's thesis]. Provo, Utah: Brigham Young University; 1989.
7. Whistler WA. *Polynesian Herbal Medicine*. Lawai, Kaua'i, Hawaii: National Tropical Botanical Garden; 1992.
8. Morton J. The ocean-going noni, or Indian Mulberry (*Morinda citrifolia*, Rubiaceae) and some of its "colorful" relatives. *Econ Bot.* 1992;46:241-256.
9. Guppy HB. *Plants, Seeds and Currents in the West Indies and Azores*. Covent Garden, London, England: Williams & Norgate; 1917.
10. Johansson JT. The genus *Morinda* (Morindae, Rubiadeae, Rubiaceae) in New Caledonia: taxonomy and phylogeny. *Opera Botanica*. 1994;122:1-67.
11. Whistler WA. Polynesian plant introductions. In: Cox PA, Banack SA, eds. *Islands, Plants, and Polynesians*. Portland, Ore: Dioscorides Press; 1991:41-66.
12. Terra GJA. *Quality of Tropical Food Products: A Multi-Disciplinary Approach*. Amsterdam, The Netherlands: Koninklijk Instituut voor de Tropen; 1966.
13. Jansen AAJ, Parkinson S, Robertson AFS, eds. *Food and Nutrition in Fiji: An Historical Review*. Vol 1. *Food Production, Composition and Intake*. Suva, Fiji: The University of the South Pacific; 1990.
14. Lucas L. *Plants of Old Hawaii*. Honolulu, Hawaii: The Bess Press; 1982.
15. Kahiolo GW. *He Moololeo No Kama'puaa: The Story of Kama'puaa*. Mookini T, Neizmen EC, Tom D, trans. Honolulu, Hawaii: Hawaiian Studies Program, University of Hawai'i; 1978.
16. Leister E. Isolation, identification, and biosynthesis of anthraquinones on cell suspension cultures of *Morinda citrifolia*. *Planta Medica*. 1975;27:214-224.
17. Degener O. *Plants of Hawaii National Park Illustrative of Plants and Customs of the South Seas*. Ann Arbor, Mich: Edward Brothers; 1945.
18. McClatchey W. *The Traditional Medicinal System and Ethnopharmacopoeia of Rotuma* [master's thesis]. Provo, Utah: Brigham Young University; 1993.
19. Zepernick B. *Arneithpflanzen der Polynesier*. Berlin, Germany: Verlag von Dietrich Reiner; 1972.
20. Handy ESC, Pukui MK, Livermore K. *Outline of Hawaiian Physical Therapeutics*. Honolulu, Hawaii: Bishop Museum Press; 1934.
21. Chun MN. *Native Hawaiian Medicine*. Honolulu, Hawaii: First People's Productions; 1994.
22. McBride LR. *Practical Folk Medicine of Hawaii*. Hilo, Hawaii: The Petroglyph Press; 1975.
23. Hirazumi AY. *Antitumor Studies of a Traditional Hawaiian Medicinal Plant, Morinda citrifolia (noni), in vitro and in vivo* [doctoral dissertation]. Honolulu, Hawaii: University of Hawai'i; 1997.
24. Dixon AR, McMillen H, Etkin NL. Ferment this: the transformation of Noni, a traditional Polynesian medicine (*Morinda citrifolia*, Rubiaceae). *Econ Bot.* 1999;53:51-68.
25. Heinicke RM. The pharmacologically active ingredient of noni. *Pacific Tropical Botanical Garden Bulletin*. 1985;15:10-14.
26. Hirazumi A, Furusawa E, Chou SC, Hokama Y. Anticancer activity of *Morinda citrifolia* (noni) on intraperitoneally implanted Lewis lung carcinoma in syngenic mice. *Proc West Pharm Soc.* 1994; 37:145-146.
27. Sugiura K, Stock CC. Studies in a tumor spectrum. III. The effect of phosphoramides on the growth of a variety of mouse and rat tumors. *Can Res.* 1955;15:38-51.
28. Hirazumi A, Fususawa E. An immunomodulatory polysaccharide-rich substance from the fruit juice of *Morinda citrifolia* (noni) with anti-tumor activity. *Phytotherapy Res.* 1999;13:380-387.
29. Hirazumi A, Furusawa E, Chou SC, Hokama Y. Immunomodulation contributes to anti-cancer activity of *Morinda citrifolia* (noni) fruit juice. *Proc West Pharm Soc.* 1996;39:7-9.
30. Wang M, Kikuzaki H, Csiszar K. Novel trisaccharide fatty acid ester identified from the fruits of *Morinda citrifolia* (Noni). *J Agric Food Chem.* 1999;47:4880-4882.
31. Wang M, Kikuzaki H, Jin Y. Novel glycosides from noni (*Morinda citrifolia*). *J Nat Prod.* 2000;63:1182-1183.
32. Liu G, Bode A, Ma WY, Sang S, Ho C-T, Dong Z. Two novel glycosides from fruits of *Morinda citrifolia* (noni) inhibit AP-1 transactivation and cell transformation in the mouse epidermal JB6 cell line. *Can Res.* 2001;61:5749-5756.
33. Fong ST, Johnson A, Ho C-T, Csiszar K. *Extracts of Morinda citrifolia (noni) exhibit selective anti-tumor activity against breast and colon carcinoma cell lines*. Poster presented at: Building Bridges with Traditional Knowledge Summit meeting; May 30, 2001; Honolulu, Hawaii.
34. Issell B. *The Noni Study*. Honolulu, Hawaii: Cancer Research Center of Hawai'i, Clinical Studies, 2001. Available at: www.hawaii.edu/crch/censtudynoni.htm. Accessed October 10, 2001.

Editorial Note

Noni has made a rapid transition from a traditional Hawaiian medicine to an NIH-funded experimental agent. Cancer patients around the country have used it. However, as McClatchey shows, the science behind the use of noni in cancer is still rather minimal. He mentions his inability to find scientific references to xeronine and proxeronine in the literature. The associate editor of *Integrative Cancer Therapies*, Charlotte Gyllenhaal, has served for many years on the staff of NAPRALERTSM, a highly reputable international database on phytochemistry and pharmacology of medicinal plants located at the University of Illinois at Chicago. We also have been unable to locate these names in NAPRALERTSM or in other chemical databases, and we remain unconvinced of the reality of these substances.