



DISTRIBUTION of the GENERA of LIVING CYCADS

- | | |
|---------------|-----------------|
| 1 ZAMIA | 5 ENCEPHALARTOS |
| 2 MICROCYCAS | 6 STANGERIA |
| 3 DIOON | 7 CYCAS |
| 4 CERATUZAMIA | 8 MACROZAMIA |
| | 9 BOWENIA |

Toxicity of Cycads

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This is a review of the literature on the use of cycads as food and medicine, with special attention to their toxic properties. In the tropics and subtropics, where the plants are indigenous, their toxicity has long been known. Both gastrointestinal and neurological effects have been reported. Although several toxic components of the plants have been investigated, none has yet been shown to be responsible for specific effects. No lesion has been demonstrated to account for the progressive and apparently irreversible posterior paralysis which reputedly follows consumption of the plants by cattle. Current interest in the toxicity of the cycads has been stimulated by recognition of the high incidence of neurological diseases in an area of the world where they are used as food.

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Introduction

Cycads belong to an ancient family which predominated over other vegetation during the greater part of the Mesozoic. They are now restricted to tropical and subtropical regions, where they are well adapted to adverse conditions and survive when other plants are destroyed by hurricane or drought. The cycad is thought to represent an intermediate evolutionary step from fern to flowering plant. Cycads belong to the family *CYCADACEAE* of the *Gymnospermae*. The nine genera are: *Bowenia*, *Ceratozamia*, *Cycas*, *Dioon*, *Encephalartos*, *Microcycas*, *Macrozamia*, *Stangeria*, and *Zamia*.

There are approximately 100 species of living cycads. Species mentioned in this paper and the abbreviations used in text and tables are given on page 272. Because the nomenclature and taxonomy of the *CYCADACEAE* are not at present in an ordered

state, botanical names are used as found in the source reference. Vernacular terms for cycads are listed to aid in identification in Appendix B (p. 294).

Often there is not even a thin line of differentiation between food plants, toxic plants and medicinal herbs. So it is with the cycads. Their nutritional value lies chiefly in an edible starch extracted from root, stem, and nut.* For peoples living where cycads are native, they provide both a staple and an emergency food. As a medicinal plant, the cycad is used for a variety of oilments. Persons familiar with the plant have long recognized that it contains a toxic ingredient and routinely take precautions in its preparation. It is held responsible for heavy losses of both cattle and sheep. For cattle particularly, continued ingestion produces an irreversible paralysis of the extremities.

Scientific interest in the role of cycads in disease is not new. Search for the plant's toxic ingredient began in the 1870's. Little progress was made until 1941, when a glycoside was isolated from *Macrozamia spiralis* (198). Several glycosides have since been isolated and found to be lethal to animals. None of these compounds have been shown to be responsible for producing locomotor difficulties. On the other hand, crude plant material fed to cattle has repeatedly produced a progressive paralysis (113, 117).

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*Throughout the text, the terms *nut* and *seed* refer to the mature seed of the cycad. In tables, as far as possible, the terms *fruit*, *seed*, *nut*, and *kernel* are taken from the original source.

Genus, Species	Abbreviations	Locale
<i>Bowenia</i>		Australia
<i>B. spectabilis</i> Hook.	<i>B. spect.</i>	
<i>B. serrata</i> F. M. Bail.	<i>B. ser.</i>	
<i>Ceratozamia</i>		C. Amer. (Mexico)
<i>Cycas</i>		Oceania, Asia
<i>C. circinalis</i> L.	<i>C. circ.</i>	
<i>C. media</i> R. Br.	<i>C. media</i>	
<i>C. pectina</i> Griff.	<i>C. pect.</i>	
<i>C. revoluta</i> Thunb.	<i>C. rev.</i>	
<i>C. rumphius</i> Miq.	<i>C. rump</i>	
<i>Dioon</i>		C. Amer. (Mexico)
<i>D. edule</i> Lindl.	<i>D. edule</i>	
<i>Encephalartos</i>		South Africa
<i>E. barkeri</i> Carruth.	<i>E. bark.</i>	
<i>E. cycadifolis</i> Lehm.	<i>E. cycad</i>	
<i>E. horridus</i> Lehm.	<i>E. hor.</i>	
<i>E. lehmanii</i> (E&Z) Lehm.	<i>E. leh.</i>	
<i>E. longifolius</i> Lehm.	<i>E. long.</i>	
<i>E. septimus</i>	<i>E. sept.</i>	
<i>E. transversus</i>	<i>E. trans.</i>	
<i>Macrozamia</i>		Australia
<i>M. douglasii</i>	<i>M. doug.</i>	
<i>M. fraseri</i> Miq.	<i>M. fras.</i>	
<i>M. heteromera</i> C. Moore	<i>M. het.</i>	
<i>M. miquelii</i> F. v. Muell. (or A. DC.)	<i>M. miq.</i>	
<i>M. pauli quihelmi</i>	<i>M. paul.</i>	
<i>M. peroffskyana</i> Miq.	<i>M. per.</i>	
<i>M. reidii</i> (Gardn.) (C. A. Gardn.)	<i>M. reid.</i>	
<i>M. spiralis</i> (Salisb.)	<i>M. spir.</i>	
<i>Microcycas</i>		Cuba
<i>Stangeria</i>		South Africa
<i>Zamia</i>		C. Amer. S. Amer. Caribbean
<i>Z. boliviana</i> (Brogn.) A. DC.	<i>Z. bol.</i>	
<i>Z. cupatiensis</i> Ducke	<i>Z. cup.</i>	
<i>Z. furfuracea</i> L. f.	<i>Z. fur.</i>	
<i>Z. integrifolia</i> (Ait.) (Rich.) (Willd.)	<i>Z. integ.</i>	
<i>Z. jirijirimensis</i> R. E. Schultes	<i>Z. jir.</i>	
<i>Z. latifoliata</i>	<i>Z. latif.</i>	
<i>Z. loddigesii</i> Miq.	<i>Z. lodd.</i>	
<i>Z. media</i> Jacq.	<i>Z. media</i>	
<i>Z. multifoliata</i> (L.) A. DC.	<i>Z. multi.</i>	
<i>Z. muricata</i> Willd.	<i>Z. muri.</i>	
<i>Z. wallisi</i> R. Braun	<i>Z. wall.</i>	

New impetus for research on cycads has been the recognition of a possible relationship between ingestion of cycad material and the occurrence of a severe paralytic condition in humans. On the island of Guam, the incidence of amyotrophic lateral sclerosis, a

neurological disease, has been found to be more than 100 times greater among the natives* than among residents of areas such as

*The native residents of the Marianas (Guam, Tinian, Saipan, and Rota) are Chamorro, a Malayo-Polynesian group (149).

the continental United States (245). The etiology of this fatal motor disease is unknown, and there is no effective treatment. In the search for causes of amyotrophic lateral sclerosis, investigations of toxic substances are presently focused on *Cycas circinalis*, which the Guamanians have long utilized as a reliable source of food starch.

This review focuses on the toxic effects of cycads on humans and animals. Material pertinent to chemical and laboratory research has been drawn from government documents and publications of chemists, veterinarians and animal specialists. Descriptions of food and medicinal use and accounts of toxic effects have been based on the reports of botanists, anthropologists, agriculturists and other observers of native practices. Such handbooks as regional floras and manuals of poisonous plants have provided basic background.

Plant Characteristics

Although the genera of cycads differ considerably, the full-grown plant of any species presents a striking appearance. Vernacular names suggest their various characteristics. Dragon tail and phoenix tail palm hint at a mythical origin, and such terms as palma corcho, palma de goma, and oliba describe physical traits. Others such as tio tamale (uncle tamale) and comfort root imply dependability. Some indicate similarity to familiar plants: sato (sago?), wild date, wild pineapple, pakis adji (big fern), and pakis laut (sea fern). Religious and magical associations are implied by such names as mod jajes (my Jesus?) palm, palma de la virgen, and ghost palm. The plant's harmfulness is inferred by ricket fern and tua wa wa nie (devil's coconut).

Cycads, which are slow growing, have two slightly different growth forms: one with a tuberous-like stem, the other with a columnar stem. The tuberous stems are either short or subterranean and are often branched. The columnar types reach a height of 30 feet or more and are seldom branched. Although cycads are considered woody plants, their stems have only a thin layer of wood. This layer surrounds a large pith or marrow and is enclosed by a heavy cortex.

The roots of cycads bear symbiotic nodules

by which they are able to absorb and utilize free nitrogen of the air. The size and depth of the roots provide the plants with support during high winds and contribute to survival when lands are burned over.

A crown of pinnately compound leaves surmounts both the columnar and the tuberous stems. The length of the leaf varies from a few inches in the smallest species to six or seven feet in the largest plant. Although the leaves give the impression of being feather-like and fragile when viewed from a distance, they are usually tough and hard with a heavy midrib and often have sharp spiny tips. Specially adapted leaf structures cut down water loss and also aid the plant in surviving on a small moisture supply.

All living cycads have cones of two kinds: pollen bearing and seed bearing. The cones, which are produced on separate plants on modified leaves called sporophylls, are arranged at the top of the stem either in loose whorls or in compact aggregations. On the male plant, pollen grains are contained in numerous sporangia along the lower surfaces of the sporophyll; on the female, two or more naked seeds are attached to each sporophyll. Seeds have an outer fleshy layer and an inner stony portion, the two portions being separated by a paper-thin membrane. Size and weight of cone and size and color of the seed appear to be constant for a given species (98).

The economic importance of cycads lies chiefly in their use as ornamentals and for decoration (96). Commercial use as a source of food, laundry starch, and alcohol has been limited. In Asian countries, wood of species of *Cycas* is valued for the manufacture of small articles, such as boxes and plates. The leaves of *Cycas revoluta*, which are high in nitrogen content, are used in the Ryukyu Islands as a fertilizer for rice, sweetpotatoes and sugar cane. After starch is extracted from the underground stem of *Zamia*, the residue is used as a fertilizer for citrus groves. Fluff or "tonder" from the base of *Cycas* leaves has been utilized in some areas for stuffing pillows and mattresses.

Cycads as Medicine

Knowledge of the healing properties of the cycad dates back many years. Similar medicinal uses of the plant are to be found

in folk lore from widely separated areas. Table 1 is a selected compilation of the common uses of the cycad in folk medicine. The majority of uses are derived from the geographically widespread genera: *Cycas* and *Zamia*.

Many of the uses recommended (for a therapeutic shampoo, a strengthener for the bath, etc.) appear to be innocuous. In contrast, beverages and teas are prescribed as purges, pain depressants and emmenagogues. These last mentioned uses suggest that the plant contains a physiologically active ingredient which, in quantities greater than prescribed, might be toxic. Characteristics of the plant which may contribute to its therapeutic value for external as well as internal use are the hardening of the exudate upon exposure to air and the astringent and mucilaginous properties of the plant sap. Cycad starch likewise has a mucilaginous quality.

As an external remedy, the grated fresh seed is recommended for the removal of old scars. The brown, woolly sporophyll, ground to a fine powder, is used as a styptic. Applications of the prepared starch, the fresh exudate or the grated fresh seed or stem reputedly have a healing effect on insect and snake bites, swellings, wounds and boils. Guamanians enthusiastically recommend the grated fresh nuts of *Cycas circinalis* for curing tropical leg ulcers; and a similar use is reported by both Pak* natives and European residents on Manus, largest of the Admiralty Islands: "The mature nut is opened and the meat scraped out. The meat is then squeezed out and the juice is allowed to run on the ulcer. This is said to cause great pain. After the juice has been put on the sore, the grated flesh is then put on it and the sore covered. This is done once a day for three or four days. . ." (113).

Medicinal beverages and teas might be classified in two types: those producing a soothing effect and those prescribed as an irritant or stimulant. However, no pharmacological or chemical research explains the

specific action of any of the medications listed in Table 1 or of other reputed uses such as antidote for poisonous bites. Natives in Mato Grosso, Brazil, relate that lizards, if they have been bitten by a cobra in a fight, neutralize the action of the venom by chewing the root of *Zamia boliviana* (36). Another tale from Florida suggests that vultures eat the root of *Zamia* sp. to assist in the digestion of tainted carcasses.

Limited use has been reported of cycad material as an ingredient in the manufacture of pharmaceuticals. It is of interest, however, that since 1960, Japanese investigators have been studying the anti-tumor effect of cycasin, a glycoside isolated from *Cycas revoluta*. Some inhibition of the growth of transplanted Ehrlich ascites carcinoma in mice has been reported, but with dosage sufficiently high to produce significant effect, the animals die from the toxic effects of the cycasin. This research continues with the study of the effects of cycasin on solid tumors and other malignant growths (237).

Food Use By Humans

Foods made from cycads are most commonly regarded as a reserve for famines, seasonal shortages and other emergencies. However, these uses do not entirely explain the lasting popularity of cycads. The people of many areas appreciate the flavor and texture of foods made from the cycad. Evidence of its high prestige is found in numerous native customs. In the Melville Islands,* the cycad is among the plants selected for first-fruit rites (150). For the Karawa** in Australia, it has an important role in initiation and other ritual ceremonies (146). In Fiji,*** all fruits of the cycad are reserved for use of chiefs (21). Tessier, in 1793, wrote that, in Japan, the cycad was so highly esteemed and closely guarded that it was not permitted ". . . on pain of death. . ." to remove the plant from the islands. Reasons for

*The Tiwi are the aboriginal inhabitants of Melville and Bathurst Islands.

**The Karawa are a tribe of Australian aborigines inhabiting the Wearyan and MacArthur Rivers of the Borroloola district of the Northern Territory.

***The natives of the Fiji Islands are Melanesians with Polynesian intermixture.

*Pak is one of the Admiralty Islands which is east of New Guinea. In 1934, there were 89 households on the islands forming a self-contained fishing and agricultural community. Pak is part of the Manus cultural group (148).

TABLE 1
CYCADS AS MEDICINE: EXTERNAL USE

Genus, Species	Plant Part	Preparation	Use	Geog. Area	Ref.
1. <i>Zamia</i>	Fruit	Mash*	As a therapeutic shampoo	Dom. Rep.	20
2. <i>C. pect.</i>	Stem	Pound	As a wash for diseased hair	India	43
3. <i>Z. multi.</i>	Roots	Extract starch	In bath to give strength	Cuba	79
4. <i>Cycas</i>	Gum		For insect bites		83
5. <i>C. circ.</i>	Gum		For snake bites	India	23
6. <i>Zamia</i>			For snake bites	Mexico	89
7. <i>C. rump.</i>	Seeds	Grate	"Removes framboesia scars, cures ulcerations."	Indonesia	35
8. <i>C. rump.</i>	Resin		"Cures malignant ulcers"	India	57
9. <i>C. circ.</i>	Seeds	Squeeze and grate	For tropical ulcers	Guam and Manus	254 113
10. <i>Zamia</i>	Stem	Extract gum	To treat ulcers	Dom. Rep.	76
11. <i>C. circ.</i>	Seeds	Roast, powder, put in coconut oil**	For wounds, boils, and itch	Philippines	74
12. <i>C. circ.</i>	Buds	Crush	For wounds, swollen glands, boils	Indochina	53
13. <i>C. rump.</i>	Stem	Chew with betel	As poultice to relieve swelling	Indonesia	35
14. <i>C. circ.</i>	Cones (female)	Crush	As poultice to relieve "nephritic" pains	India	57
15. <i>C. circ.</i>	Bark, seeds	Make tincture, or grind to paste and mix with coconut oil.	As poultice for sores and swelling	India	160
16. <i>C. rev.</i>	Mega- sporophyll	Grind	To stop bleeding	W. China	37
17. <i>C. rev.</i>	Fruit	Boil in water	As an expectorant	China	87
18. <i>Zamia</i>	Roots	Chew	To relieve cough and improve singing voice	Guatemala	93
19. <i>C. rev.</i>	Seeds	Make a tincture	For headache, giddiness, and sore throat	India	160
20. <i>C. rump.</i>	Seeds		For asthma	Malaya, Indonesia	12 35
21. <i>C. rump.</i>	Leaves	Squeeze	To check hematemesis, to relieve colic	Indonesia	35
22. <i>C. rev.</i>	Seeds		As an emmenagogue and astrin- gent, dose "10-20 g per day"	Ryukyus, S. Japan	61
23. <i>C. rev.</i>	Seeds	Use raw	To check diarrhea	Oshima, Ryukyus	247
24. <i>C. circ.</i>	Fruit	Mix with sugar	As a laxative	India	23
25. <i>C. circ.</i>	Seeds	Boil starch	For hemorrhoids and dysentery	Ceylon	62
26. <i>C. rump.</i>	Fruit	Boil	As an emetic	Indonesia	35
27. <i>Z. muri.</i>	Sap	Squeeze fruit	As a drastic purge	Venezuela	76
28. <i>C. circ.</i>	Stem	Extract starch	As a "strengtheners and restorative"***	India, Europe	10
29. <i>C. rev.</i>	Fruit		As a tonic, "produces plumpness"	China	87
30. <i>D. edule</i>	Seeds	Make decoction	To relieve neuralgia	Mexico	89
31. <i>C. circ.</i>	Male bracts	Mix with sugar	As an aphrodisiac and stimulant	India	57
32. <i>C. circ.</i>	Scales		As an anodyne, "dose 30-60 grains or more"	India	100
33. <i>C. circ.</i>	Male bracts		As a "narcotic"	India	57

*Fry in oil and mix with mashed mamey and avocado seeds.

**Or in a clay suspension.

***Sold as tonic in Europe.

the official edict were twofold: the plant provided an excellent ration for soldiers living off the land; and by attempting to restrict the cycad to Japan, the government hoped to deprive enemies of its use (165).

All parts of the plant of one or another species of cycad are used as food.* A selection of the various uses is presented in Table 2. In Guam, the green outer husks of seeds of *Cycas circinalis* are chewed to relieve thirst and, when dried, are considered a tasty sweet. Similar use of the seed husks is reported in Australia for *Cycas media*. The raw gum or exudate of a species of *Encephalartos* is chewed by children in some areas of Africa. In Indonesia, Ceylon, and the Philippines, the succulent leaves and tender shoots of *Cycas rumphius* are used as greens and in curries. The green fruit can be boiled or roasted to edible softness; the white meat has a flavor and texture which have been compared to that of a roasted chestnut (10). After a period of soaking, the mature kernels can be boiled or roasted; Australian settlers called these "blackfellows' potatoes"

(123). According to reports from different geographical areas, the fruits of *Cycas circinalis* are thinly sliced, dried and used as a conserve or jam (35).

A high-quality food starch is extracted from the fibrous pulp of cycads through alternate processes of cutting, drying and soaking.* In the most commonly reported method, cutting and soaking precede the drying process. Prior to use, the hard dry pieces are ground to a fine powder. This is the general order of procedure in Guam, India, Indochina, Indonesia and East Africa. Variations are reported from other areas. In Western Australia, the starchy portion (pith of *Macrozamia*) is first dried, then pounded and soaked. The extracted starch is later alternately dried and pounded until a fine powder is obtained (33). In Queensland and New South Wales, Australia, and in Ishigaki in the Ryukyu Islands, the seeds (*Cycas media* and *Cycas revoluta*) are halved, dried, grated and then washed in running water for 24 hours or longer (64, 50, 29). Variations in the order of the procedures for starch extraction may be related to such factors as species, portion of the plant, weather conditions during the processing season and utilization of the starch. The consequences of these variations as regards the safety of the final product have been questioned. Nishida's experiments have shown that more of the toxic substances are removed if pounding

*Proximate Composition
(Fat content less than 1%)

	% Starch	% Protein	Ref.
<i>Cycas revoluta</i>			
kernels, fresh	33	7	247
kernels, dry	60	12	247
pith	41	7	183
outer husk of seed, fresh	21	4	191
outer husk of seed, dry	46	10	191
<i>Macrozamia spiralis</i>			
kernels, fresh	53	6	198
kernels, dry	67	neg	170
leaves, fresh	13	3	170
leaves, dry	57	11	170
<i>Zamia</i> , sp.			
root, air dried	38	6	175

*Large containers are needed for soaking the cycad nuts. In Guam, 50-gallon drums have been in common use since 1930, when the first air bases were built. Many of these drums were containers for high-test gasoline. In preparing the drums for use, the interiors are burned out and then often painted with red lead to prevent rust and corrosion (254).

TABLE 2
CYCADS AS FOOD FOR MAN: A. UNCOOKED

Portion	Species	Preparation and Use	Area	Ref.
1. Husk	<i>C. circ.</i>	Eat green or dried.	Guam	254
2. Husk	<i>C. media</i>	Eat "raw."	Australia (Karawa)	146
3. Fruit	<i>C. rev.</i>	Grind to a paste for a spread on bread.	Ryukyus	252
4. Fruit	<i>C. circ.</i>	Eat with sugar	India	23
5. Seeds	<i>C. circ.</i>	Slice thin, dry, use as conserve or jam.	Indonesia	35
6. Gum	<i>E. sp.</i>	Chew.	Africa	96

TABLE 2 (continued)
CYCADS AS FOOD FOR MAN: B. BOILED OR ROASTED

Portion	Species	Preparation and Use	Area	Ref.
7. Shoots, leaves	<i>C. rump.</i> <i>C. circ.</i>	Boil as vegetable and for curries.	Java, Sumatra, P. I., Ceylon	35, 62 30
8. Y. leaves	<i>Z. wall.</i>	Boil as vegetable.	Colombia	68
9. Fresh kernels	<i>C. media</i>	Soak to remove caustic property, cook in hot ashes.	Australia (Karawa)	146
10. Seeds	<i>D. edule</i>	Roast or boil.	Mexico, Honduras	89, 95
11. Ripe Seeds	<i>C. circ.</i>	Boil kernel until soft.	Fiji	21
12. Nuts	<i>M. sp.</i>	Bake.	Western Australia	33
13. Rhizomes	<i>B. spect.</i>	"Cook."	Australia	3, 151
14. Roots	<i>Zamia</i>	Scrape or peel and boil. Drain and mash. Cook with meat and vegetables for a stew called "sofkee."	Florida (Seminoles)	56
CYCADS AS FOOD FOR MAN: C. DRY STARCH				
15. Kernels	<i>C. rev.</i>	Cut in very fine pieces, soak 3 days in running water, dry thoroughly.	Indochina	73
16. Seeds	<i>C. rump.</i>	Cut, steep in sea water for a few days, sun dry, pulverize, steam in a basket, mix with brown sugar and grated coconut ("kooyaboo").	Indonesia	60
17. Seeds	<i>C. circ.</i>	Cut, soak for some days with at least 3 changes of water, sun dry and preserve for later use.	Guam, Marianas	162
18. Seeds	<i>C. circ.</i>	Break or grate, soak for several days changing water from time to time, sun dry, grind, bake on a hot griddle like a tortilla.	Guam, Marianas	80
19. Seeds	<i>C. circ.</i>	Split, soak,* dry, and grind. Use to thicken "aho," a sweet soup. Mix with coc. milk or fermented coc. sap and cook on griddle ("tortilla"), or wrap in banana leaf and steam or boil ("babinka").	Guam, Marianas	254
20. Pith	<i>C. circ.</i>	Pound, soak, settle, dry.	Indochina	107
21. Pith	<i>C. circ.</i>	Saw in pieces, beat in mortar, soak, settle, strain through a cloth, dry, make into cakes.	India	10
22. Seeds	<i>C. circ.</i>	Dry for month. Pound.	India	23
23. Stem	<i>E. sp.</i>	Dice, soak, dry 3 days, pound, cook or bake.	E. Africa (Giryama)**	157
24. Under-ground stem	<i>Z. sp.</i>	Scrape or peel, and boil until soft. Mash, drain and dry in sun.	Florida (Seminole)**	56
25. Under-ground stem	<i>Z. cup. and Z. jir.</i>	Use as starchy meal or farina.	Colombian Amazon	82
26. Seeds	<i>C. rev.</i>	Cut in half, dry in sun, grate, wash with constantly changing water for 24 hours.	Miyako, Ryukyu Islands	29
27. Kernel	<i>C. media</i>	Break, dry, soak in dilly bag in water for several days. Pound, roast, and pound several times. Use as starch.	Queensland, Australia	64
28. Seeds	<i>C. media</i>	Break, sun-dry for 3-4 hrs., soak in running water for 4-5 days. Pound. Bake cakes under ashes.	New South Wales, Australia	50

* One person advises 18 days with at least 4 changes of water.

**The Giryama are a tribe of the Nika (Wanyika) nation in Kenya. The Seminole are a tribe of the Creek (Muskogee) Indian Confederacy (149).

TABLE 2 (continued)
CYCADS AS FOOD FOR MAN: D. FERMENTED

Portion	Species	Preparation and Use	Area	Ref.
29. Seeds	<i>C. media</i>	Slice, sun dry, soak for several days, tie up in ti-tree bark to ferment.	Australia	51
30. Kernels, husks	<i>C. media</i>	Dig large trenches about 20' long, 2' wide and 1' deep. Line with grass. Break nuts open out of shell into trench in layers. Cover with earth. Dig up after 2-3 months. Pulverize on grinding stones. Moisten powder with saliva and bake in slabs about 7"x3"x1". Cook in hot ashes. With paper-bark cover, starch is readily transportable for trade and ceremony ("mundja").	Australia (Karawa)	146
31. Seeds	<i>C. circ.</i>	Split, sun dry about 4 days, ferment in a tin with layers of banana leaves for a week, remove mold, soak another day, powder. Use as porridge.	Africa	103
32. Large ripe fruit	<i>C. circ.</i>	Split, sun dry about 4 days, ferment in a tin with layers of banana leaves for a "long time." Boil as veg. with coc. cream.	Africa	103
33. Stem	<i>E. sp.</i>	Wrap pith in animal skin for two months, knead, make into cakes and bake in embers ("Kafir bread").	South Africa	166
34. Stem	<i>E. trans.</i>	Slice, bury, dry, crush for use in porridge.	Africa	96
35. Stem	<i>E. sp.</i>	Chop, ferment for a week, wash (preferably in hot water), dry in sun, pound, make into a thick porridge ("ugali"). Bury for one month.	Africa	103
36. Red rind of nuts	<i>M. sp.</i> "quenine"		Western Australia	22
37. Nuts and pulp encasing nuts	<i>M. fras.</i>	Soak in shallow pool 7 days, bury in holes (about 12" in diam., 36" deep) which have been lined with rushes. Sprinkle with a little sand. Cover with tops of the grass-tree. Use after fortnight when outer pulp encasing nut is dry.	Western Australia	51
38. Seeds	<i>M. mig.</i>	Pound, put in dilly bag, soak in stream or water hole about 6 days until mass is reduced to a paste, then bake in ashes.	New South Wales, Australia	137
39. Roots	<i>Z. sp.</i>	Peel, grate (on tin grater), catch pulp in bowl of salted water, squeeze dry in cloth, add salt, wrap in plantain or "almendra" leaves.	Florida (Seminole)	153
40. Stem	<i>C. rev.</i>	Cut into 1/2" slices. Sun dry for few days. Soak until piece can be easily bent. Dry and "brew" in a straw bag. Wash well and pound. Can be used like rice.	Oshima, Ryukyu Islands	247
41. Stem	<i>C. rev.</i>	Cut in small pieces. Alternately dry and ferment for 20-30 days, pound, add water and decant several times. Use damp starch for dumplings. Sun dry for 1-2 days and store. Eat as porridge "dogaki."	Oshima, Ryukyu Islands	247
42. Seeds	<i>C. rev.</i>	Split seeds and husk. Dry in sun. Remove kernel from shell. Dry until hard and store in straw-bag or box. Before use, wash and pound. Mix with dried crushed sweet potatoes or ferment for miso ("yandbu malt miso" or "nari malt miso").	Oshima, Ryukyu Islands	247

and drying take place prior to the soaking. Detoxification may also be aided by fermentation (188).

Although some fermentation usually accompanies starch extraction, fermentation itself is a method of preparing highly prized

foods and beverages. Westerners have compared the flavor of fermented cycad seeds with that of some of the best-known European cheeses (150). Seeds of *Cycas revoluta* are often used as the basis for sake in the Ryukyu Islands (145). Stems of *Encephalartos septimus* are employed in making beer in some regions of Africa (151). Throughout the Caribbean area, one of the seasonal delicacies is a product of fermented *Zamia* starch. The freshly extracted starch is made into loaves or balls about 16 inches in diameter. These are allowed to ferment for a few days. When the ball is broken for use, the starch has a dark color, and the interior of the ball is filled with maggots. Unless the starch is black and wormy, it is considered fatally poisonous and unsuitable for food (20, 153). Other fermented foods are prepared by soaking cycad pulp in a still pond or burying in a trench lined with grass and leaves. Animal skins or banana leaves used to wrap the pulp during the burial period may provide sufficient tannic acid to aid the detoxification process.

In some localities, the production of fungi appears to be an important step in the fermentation process. Nishida reported that, in Oshima in the Ryukyu Islands, dried slices of cycad pith (*Cycas revoluta*) were placed in a bag and stored indoors for 20 to 30 days. Every fifth day they were sunned for about half a day. Fungi grew on the slices. At the end of the period, the slices were soaked in water for a few days, until each piece could be easily bent. Slices were then dried in the sun for a few hours, pounded in a mortar and alternately soaked and decanted several times. With this process, Nishida considered that the pith was completely fermented and detoxified (188). In 1955, Kobayashi, on an inspection tour of Oshima, observed that small pieces of the cut stem were left for some time under a straw mat to promote the growth of a "black fungi" (243).

One of the advantages of cycad starch is that, when thoroughly dried, it can be stored for long periods. In Guam, the hard dry pieces of sliced seeds (*Cycas circinalis*) are kept from season to season. Prior to use, they are ground to a fine powder, which provides starch for a variety of cooked dishes, including tortillas, cakes, and soups (254).

The Karawa wrap the dried slices of *Cycas media* seeds in cylinders of paperbark for trade use and as a food reserve (146). In the Ryukyu Islands, moist starch (*Cycas revoluta*) is often mixed with rice and made into small cakes which are dried and stored for later use (247).

Starch-making from cycads is both a home and a commercial industry. According to a report of 1925 on Oshima in the Ryukyu Islands, the annual harvest of cycad seeds for starch-making was estimated at 230 tons (*Cycas revoluta*) (247). A later survey, made in 1931, showed that the island residents consumed 90 percent of their starch production. The remainder was shipped to the metropolitan areas of Okinawa and Japan* (247). Reports from Guam indicate that food starch produced on the island (*Cycas circinalis*) is sold, traded and used as gifts among Guamanians living on islands of the Marianas and in the United States* (254). In the Dominican Republic in 1954, it was estimated that 10 to 15 tons of *Zamia* root (*Zamia* (?) *media*) were processed each year for local markets* (20). Although cycad starch is no longer manufactured on a commercial scale in the United States, it was a pioneer industry in southern Florida as early as 1845. At the peak of production, mills along the Miami River processed approximately 10 to 15 tons of *Zamia* root weekly. Most of this starch, which was marketed under the name Florida arrowroot, was used for infant foods, biscuits, chocolates, and spaghetti (71).

Effects on Humans

We find recurring accounts of ill effects from eating the plant accompanying the reports of the use of the cycads as medicine and food. Casualties most frequently occur during periods of extreme food shortage. The cause of the ailments can often be traced to inadequate preparation of cycad products. This may be due either to lack of knowledge of the toxicity of the plants or to their unpredictable variations in toxicity. From at

*Cycad starch is marketed in Japan under the name sotetsu; in Guam, as asciento federico or asciento fadang; and in the Dominican Republic as guayiga.

least one locality, Oshima in the Ryukyu Islands, there are reports that some nuts have greater toxicity than others and that occasionally a batch kills all who eat or drink the product (145).

The ailments range from minor and vague complaints to severe and often fatal illnesses. Symptoms include: headache, violent retchings, vertigo, swelling of the stomach and legs, depression, stupor, euphoria, diarrhea, abdominal cramps, tenesmus, muscle paralysis and rheumatism. Some of these symptoms are acute immediately following ingestion of cycad products. In other cases the relationship between the ingestion of the cycad and the ailment is more difficult to define. There are virtually no well documented laboratory and clinical data to explain the physiological reactions. Table 3 shows the variety and severity of the symptoms.

Rumphius reported that ". . . in Celebes in accordance with the custom of the land, the sap from the kernels . . . (*Cycas circinalis*) . . . was given to children to drink in order to kill them so that the parents would not be hampered when they went to follow their roving life in the wilderness of the forest. . ." (35). Other accounts suggest that political enemies may have been eliminated in a similar fashion with the addition of lethal cycad starch to ceremonial dishes. Standley reported that *Zamia* root (*Z. furfuracea*) was used in Honduras as a poison for criminals and in Costa Rica for both criminals and enemies. He quoted a popular belief in Honduras that, if the root is out of the ground two days, it will kill the victim in two days; if out of the ground one week, death will occur in one week, and so on (92).

Explorers and early settlers frequently suffered as a consequence of experimentation with unfamiliar native foods. Banks, the botanist who accompanied Captain Cook on his voyage to Australia in the 1770's, reported that the crew, observing shells of cycad nuts (*Cycas media*) around camp fire sites, concluded that the natives used the plant for food. Members of the crew became violently ill following their eating of the nuts (161). In reporting a serious illness from cycad poisoning, Jones wrote that settlers' children in Australia frequently experimented with fresh *Macrozamia* nuts but

that ". . . no native would consider eating . . . (one) . . . until it had been buried for at least a month. . ." (121).

Even in areas where the cycad is in common use and its potential danger is well known, there are occasional reports of both severe illness and death resulting from hurried and careless preparation. In 1898, Fitzgerald reported that, in Madagascar, it was well known that unless cycad starch (*Stangeria* sp.) was carefully prepared, it would cause fatal diarrhea and vomiting (157). Japanese soldiers who lived in the Guam hills from the end of World War II until their surrender in 1962 have described their fright and panic when they became acutely ill following consumption of inadequately washed cycad nuts (*Cycas circinalis*). In this instance, necessity and hunger led to the use of a food about which there had been adequate warning in a Japanese military handbook (244).

In the cases and circumstances that have just been discussed, the symptoms have been acute and of varying severity and have immediately followed ingestion of cycad products. Considerable information has been collected concerning symptoms that do not appear immediately but result reputedly from ingestion of cycad products over long periods. Old Spanish letter books record the complaints of several early Governors in Guam to their Captain-General in the Philippines about the harmfulness to the native population of continued use of starch made from *Cycas circinalis*. In 1905, Safford of the United States Navy wrote that Guamanians were well aware that cycad starch was injurious to health if consumed for any length of time (80). Even today some residents of Guam attribute a variety of ailments, including lytiko,* to the handling and consumption of cycad plant material (254).

Food Use By Animals

Many animals show a preference for cycad material over other available foodstuffs. Chamberlain reported that, while he was in

*This term is common parlance for an incapacitating paralysis, many cases of which are diagnosed as amyotrophic lateral sclerosis.

TABLE 3
CYCADS: TOXIC EFFECTS ON HUMANS
(Arranged chronologically)

Genus, Species and Part of Plant	Place	Description (Adapted from source)	Ref.
1. <i>C. circ.</i> (nuts)	Queensland and north- ern Australia	A number of Captain Cook's men, during their explorations in the Pacific, suffered a strong fit of vomiting from eating cycad nuts. (1770)	161
2. <i>M. spir.</i> (fruit)	Port Johnson, Australia	Although this plant formed part of the diet of aborigines, sailors became ill with vertigo and violent retchings after eating the fruit. (Perouse's exped. 1789).	13
3. <i>C. media</i> or <i>M. fras.</i> (nuts)	Australia	Men ate nuts which were not completely dried. Seized with fits of vomiting, accompanied by vertigo and other distressing symptoms. Symptoms abated during the night, and in the morning the men were able to continue the march. (Grey's exped. 1837).	13
4. <i>C. media</i> (nuts)	Australia	Consumption of nuts caused emetic symptoms. (Leichardt's exped. 1847).	38
5. <i>Zamia</i> spp. (roots)	Florida	Northern soldiers who ate bread made from roots were afflicted with a swelling of the stomach and legs. Death followed within a short time. (1860's).	153
6. <i>M. spir.</i> (nuts)	New South Wales, Australia	14 year old boy and girl suffered vomiting and consequent depression after eating nuts. (Report of own experience).	105
7. <i>M. spir.</i> (nuts)	New South Wales, Australia	"Fern" nuts were eaten by d. of Mr. Morrison. Physician found her ". . . suffering from congestion of posterior portions of right and left lungs, quick respiration, flushed countenance, pulse 120, no change in pupils. . ." (News letter, 6 Sept., 1871).	105
8. <i>M. spir.</i> (nuts)	New South Wales, Australia	Child ate one or more nuts. Remained in a dangerous state for some time. Symptoms—violent vomiting, stupor, yellowish appearance of eyes. (News letter from Brown, 5 Sept., 1871).	105
9. <i>M. spir.</i> (nuts)	New South Wales, Australia	Men experienced ". . . severe suffering like sea-sickness, diarrhoea, and cramps in the abdomen. . ." (Melford's exped. 1876).	174
10. <i>M. sp.</i> (nuts)	Bridgton, Western Aus- tralia (near Bunbury?)	After eating "zamia" nuts, child had high temperature lasting a few days, constipation, and paralysis of muscles from the lumbar region downwards corresponding in cattle from the loin over the rump and downwards to the muscles covering the shank bone. (q. letter in Southern Times, Bunbury, 26 July, 1894).	121
11. <i>M. per.</i> (kernels and testa)	Springsure, Queensland, Australia	The kernels and testa produced symptoms of enteritis in three boys. (1890's).	51
12. <i>E. long.</i> (nuts)	Africa	". . . these dates poisoned some persons attached to a 'Boere' Commando during the Anglo-Boer War . . . not all those who had partaken of the 'dates' became ill. . ." (1890's).	135
13. <i>E. cycad.</i> (nuts)	Africa	Two Pondo lads were suspected to have been fatally poisoned by the "nuts." (q. Juritz 1914).	135
14. <i>C. circ.</i> (starch)	Guam, Marianas	During World War II, three adults in one family became violently ill after eating starch prepared from nuts soaked for a period shorter than usual (or perhaps insufficiently dried). All members of the family recovered following dosage with coconut oil. Symptoms included headache and stomach cramps.	254
15. <i>C. rev.</i> (starch)	Ryukyu Islands	Following World War II, several persons are reported to have died and others to have become acutely ill from eating improperly prepared cycad starch. A physician describing his own experience said he broke into perspiration, vomited, and lost consciousness.	29
16. <i>C. rev.</i> (starch)	Ryukyu Islands	Five persons died, one recovered following use of inadequately washed and dried starch. Medical records available. (Nov. 12, 1956).	136
17. <i>C. circ.</i> (seeds)	Guam, Marianas	Because of food shortage, Japanese soldiers, hiding in the jungle, ate inadequately prepared seeds. Entire group were ill with vomiting, tenesmus and bloody diarrhea. (1950's).	242 244

Africa, gibbons interrupted his botanical collections of *Encephalartos* carrying away the cones of the plant just as the seeds reached maturity (18). The discovery of caches containing the husk and hard kernel of seeds of *Encephalartos* has suggested that wild animals consume the fleshy portion surrounding the kernel (135). Stores of the nuts of *Macrozamia spiralis* have been found in hollow logs in New South Wales and Queensland (51). Standley reported that *Dioon edule* was a favorite food of bears and peccaries in Mexico (89). Santa Maria, also referring to *Dioon edule* in Mexico, has indicated that hogs prefer the seeds, and that cattle relish the young green shoots appearing after spring rains (131).

There are reports from Indochina that wild animals often damage the bark of the local cycads (*Cycas circinalis*) in order to obtain the fresh marrow. The pulpy residue remaining after the extraction of cycad starch is commonly fed to domestic animals in Indochina and in the Dominican Republic (107, 20). In commercial ventures in Western Australia, pith of *Macrozamia* stem and root was ground and boiled to a thick jelly-like paste and used as feed for pigs, poultry and calves (141).

It is often heard in Australia that cattle and sheep not only selectively graze various species of cycads but that some animals become "addicted" and will travel long distances for the plant. The "addicted" animals "teach" others of the herd to eat the cycad leaves. Stock losses result, and the only practical solution is to remove all "Zamia"* eaters from the group or to move the entire herd to land without cycads. Nadkarni has stated that the male bracts of *Cycas circinalis* contain an ingredient that appears to intoxicate insects that feed upon them (57).

Effects on Animals

Cycad poisoning presents a serious economic problem to cattlemen and graziers in tropical and subtropical regions. Thousands of cattle and sheep have been afflicted, and many acres of valuable range land have had to be abandoned because of expense and dif-

ficulties in controlling cycads. Various genera and species of cycad have been implicated. In Australia, *Bowenia*, *Cycas*, and *Macrozamia* are considered responsible; in Australian New Guinea, *Cycas circinalis*; in the Dominican Republic and Puerto Rico, *Zamia*; and, in Mexico, *Dioon edule*.

Stock losses are most commonly associated with the expansion of grazing into the natural habitat of cycads. Outbreaks of cycad poisoning have been known in Australia since the beginning of the vast sheep and cattle industry in the 19th Century. A selection of reports of the Australian outbreaks is presented in Table 4. According to one of the first reports, 200 head of cattle were lost in the Saltash District in New South Wales between 1879 and 1884. For the next 15 years, only occasional cases were recorded in this district; and then, in 1890, one station reported the loss of 30 head (Table 4, No. 1). Although a few deaths occurred in the Tabulam District around 1882, a major outbreak was reported in 1900 with 400 of 900 head dying. The area was then abandoned until 1912, when many fatalities followed the renewed use of the range land (Table 4, No. 2). Stock losses from cycad poisoning reached their peak in Australia in 1930. The extension of pastoral development in recent years has curtailed the access of the stock to cycads.

As pointed out by Cleland in 1914, two different effects follow ingestion of the cycad material by sheep and cattle (110). One effect is an acute condition characterized by severe gastrointestinal disturbances; the other is a partial paralysis. The most thorough investigation of an outbreak of the acute condition was Seddon's study of an incident at Coonabaraban, New South Wales, in which travelling sheep consumed ripe seeds of *Macrozamia spiralis*. Five sheep were found dead 18 to 20 hours after ingestion. Sixty to 80 deaths occurred daily for the next week; then deaths began to fall off to a few a day. Of two flocks totalling 6000 sheep, a total of 2200 died (Table 4, No. 9) (133).

The first observable signs of paralysis are a slight staggering or weaving gait and a tendency to a crossing of the hind legs in walking. No fever is reported, and the ani-

*"Zamia," a term derived from *Macrozamia*, is commonly used in Australia to refer to any of the local cycads.

TABLE 4
CYCAD POISONING: REPORTS OF OUTBREAKS AMONG CATTLE AND SHEEP

Genus, species, Vernacular	Portion of Plant	Animal	Place, Date, Losses and Comment	Ref.
1. <i>M. sp.</i> "burrawang" "zamia"	Leaves and sprouts	Cattle	Saltash Dist., New South Wales 1879-1884 ----- Over 200 head lost. 1884-1888 ----- A few losses occurred. Jan. 1890 ----- 30 head lost.	106
2. <i>M. miq.</i> or <i>M. spir.</i>	Leaves	Cattle	Tabulam Dist., New South Wales ca. 1882 ----- Occasional losses reported from hind-quarters' paralysis.	125
		Steers	1900 ----- 400 of 900 died. Addicts taught others to eat cycads. Loosening of horns noted.	
		Cattle	1900-1912 ----- Leases were renewed and many fatalities were reported.	
3. <i>M. miq.</i> and <i>M. (?) spir.</i>	Young shoots	Cattle	Near Rockhampton, Queensland 1895 ----- Many died from paralysis of hind-quarters.	122
4. <i>M. sp.</i>	Fresh leaves	Stock	New South Wales 1895 (winter) Stock became paralyzed while grazing in a pad- dock where cycads grew. Cattle were removed; cycads were cut down and left lying on the ground.	123
	Old leaves and roots		1896 (winter) Stock were returned to paddock. Within 6 weeks, many animals were para- lyzed. Stomach contents included cycad leaves. Paddock closed.	
	Old roots		1897 (winter) Heavy losses reported. Losses continued. Leases given up in April 1898.	
5. <i>M. fras.</i>	Leaves	Bullocks	Western Australia 1898 ----- 24 bullocks died after lying for a few days in a helpless and semi-para- lyzed condition.	38
6. <i>M. (?) spir.</i> "burrawang"	Leaves	Cattle	Moruya District, New South Wales 1899 ----- About 100 head were lost. Both sexes, over six months of age, were affected by a progressive and irreversible paralysis of hind quarters.	134

TABLE 4 (continued)
CYCAD POISONING: REPORTS OF OUTBREAKS AMONG CATTLE AND SHEEP

Genus, species, Vernacular	Portion of Plant	Animal	Place, Date, Losses and Comment	Ref.
7. <i>M. het.</i>	Leaves (?)	Cattle	Coonabarabran, New South Wales 1916 Animals staggered and finally lost power in hind quarters. <i>Macrozamia</i> was the only green plant in paddock. "Some" fatalities reported.	38
8. <i>M. sp.</i>	Leaves	Bullocks	Kempsey, New South Wales 1920 About 50 fatalities were attributed to <i>Macrozamia</i> poisoning.	38
9. <i>M. spir.</i>	Ripe nuts on ground	Merino ewes	Coonabarabran, New South Wales May, 1929 Sheep ate greedily for 1 hour. Five died within 18-20 hrs.; deaths continued for about 3 weeks. Diagnosed as toxic haemoglobinaemia and acute enteritis.	133
10. <i>Z. integ.</i> or <i>Z. latif.</i> and <i>Z. media</i>	Shoots and leaves	Dairy herd	Dominican Republic 1930s Within 3 weeks, 11 of 35 were paralyzed ("der-rengado"). Two mild cases recovered. No new cases developed when herd was moved to other pasture or in this pasture after <i>Zamia</i> was destroyed.	129

*1,850 of 6,000 animals died. Animals, hand fed from June 1928 to March 1929, were strong and in good health.

mal continues to have normal appetite until the last stages of the disease. These difficulties generally occur in cattle, affecting all ages and both sexes. The condition is reputed to be more common among males than females, but the exposure rate is not always apparent from the available reports.

The spasmodic nature of the outbreaks and the varied conditions under which paralysis occurs have led to considerable controversy over the circumstances under which animals are affected. Well nourished as well as poorly fed stock suffer. Stewart observed that many animals were not afflicted at a time when they were in poor condition but were when they were thriving (134). A lower incidence is reported among cattle from a paralysis-free area than among those raised from an early age in the area of the

disease (Table 4, No. 10). Plants of the same species of cycad growing in different soils appear to vary in their toxicity. Lamb reported a higher incidence among cattle that were grazing on cycads growing on swampy land than among those who were consuming cycads on the ridges (122). There is evidence that old roots and leaves that have been on the ground for as long as two years retain their toxicity and produce paralysis (Table 4, No. 4). Other factors subject to discussion are the maturity and part of plant.

Numerous feeding experiments have been conducted to evaluate the disputed conditions under which cycad paralysis occurs. However, the majority of the tests employed a single animal. Few, if any, of the experiments were carried out under controlled con-

ditions which would take into consideration such factors as infections, toxins and nutritional deficiencies, any one of which could produce locomotor difficulties. One can not be sure that the test animals were not exposed to other risks. A review of this work has value, however, in that it points up the complexities of animal research with toxic plants. This value can be appreciated from study of experiments reported by Hall and Everist in which cattle were fed cycad leaves from different sources and in different stages of growth and freshness (115, 117, 113). Their results were inconclusive. Analysis of their procedures shows that the following variables were implicated: leaves from *Cycas* and *Macrozamia*; "fresh" and "dry" leaves; "young" and "more mature" leaves; leaves from each of four geographic areas: Gympie, Fraser's Island, Toogooahawah, and Ingham; leaves collected and fed during each of three years: 1939, 1952, and 1953; and supplementary feeding of lucerne and bush hay. Steers and heifers were used in the experiments. Both paralysis and no effects were reported with each of these variables. For example, one animal developed paralysis, while another showed no ill effects from eating dried cycad leaves.

Over the past hundred years, the serious animal losses attributed to cycad poisoning

have aroused considerable concern among a wide variety of specialists whose chief interests were agricultural. The literature contains numerous accounts of their observations, many of which are based upon local hearsay. Taken together, these observations represent a wide range of beliefs concerning the toxicity of cycads. Table 5 provides a selection of these accounts arranged as they relate to the production of acute effects and paralysis.

Chemical Research

Chemical studies on cycads have focused on the isolation and identification of toxic constituents of the plants. Early investigations carried out in Australia in the late 19th Century were directed toward such substances as resin, mucin and oxalic acid. Around 1900, the Dutch government in the East Indies responded to popular demand for study of the harmful components of seeds of *Cycas circinalis*, a common source of edible starch in the islands. Work was carried out in Holland by Van Dongen who isolated an "amorphous nitrogen-free glycoside," which he named pakoein (168). According to Hurst, Guthrie suggested in 1917 that the concentration of fibre in the plant was sufficiently high to account for the ill effects in cattle (38). Nishida reported that, in

TABLE 5
CYCADS: TOXIC EFFECTS ON ANIMALS

<i>Acute effects, often ending fatally</i> (Ref. 79, 83, 101, 117, 133, 139, 140, 142, 153, 168, 174, 198, 241)	
Genera:	<i>Bowenia</i> , <i>Cycas</i> , <i>Encephalartos</i> , <i>Macrozamia</i> , <i>Microcycas</i> , and <i>Zamia</i> .
Portions:	Fresh shoots, sprouts, stems, roots, leaves, seeds, kernels, mucilage, and male bracts Dried seeds and leaves Boiled seeds Wash water from roots and seeds Residue from seeds Starch made from seeds and from stems Pakoein and macrozamin*
Animals:	Cattle, sheep, goats, dogs, cats, and pigs Fowl including chickens, turkeys, and ducks Bird including <i>Urunloca domestica</i> , pigeons, and quail Fish Rabbits, guinea pigs, rats, and mice
<i>Chronic effects with paralysis</i> (Ref. 15, 38, 101, 113, 117, 120, 129, 130)	
Genera:	<i>Cycas</i> , <i>Macrozamia</i> , <i>Zamia</i>
Portions:	Fresh inflorescence, shoots, sprouts, bulbs, leaves, and seeds Dried leaves
Animals:	Cattle, sheep, hogs, and horses

*See Table 6.

1922, Yoshimura detected formaldehyde in the seeds of *Cycas revoluta* and considered this substance responsible for the toxic effects in humans consuming the starch (182). Nishida, in 1935, produced formaldehyde from *Cycas revoluta* by the action of emulsin, which is present in the seeds (184). Seddon, following investigations of sheep poisoned by seeds of *Macrozamia spiralis*, concluded that the active principle was a ". . . specific protoplasmic poison . . . (with) . . . selective action on endothelial cells" (133). In 1941, Cooper isolated, from seeds of *Macrozamia spiralis*, a crystalline compound which was named macrozamin (198).

World War II interrupted investigation on cycads, but it was resumed soon after the war. In 1949 and 1951, Langley, Riggs, and Lythgoe, working on Australian species, proposed a methylazoxy-methanol ($\text{CH}_2\text{N}:\text{N}(\text{O})\text{CH}_2\text{O}$) structure for the aglycone of macrozamin and identified the sugar of the glycoside as primeverose (202, 205). Macrozamin was isolated from several other genera (*Cycas*, *Bowenia* and *Encephalartos*) and from other species of *Macrozamia* (210). In 1956, Riggs obtained a substance, similar but not identical to macrozamin, from *Cycas circinalis* seeds from Guam (218). In this post-war period, Nishida and colleagues isolated a glycoside, cycasin, from

seeds and pith of the Japanese species *Cycas revoluta* (212, 214). In spite of a difference in melting point, Riggs considered this glycoside identical with the one he obtained from *Cycas circinalis* (218). Subsequently, macrozamin and cycasin were shown to have the same aglycone but different sugar components (212). Additional glycosides with the same aglycone have since been isolated from *Cycas revoluta* by Nishida and colleagues. A chronological record of the research on the isolation and identification of the cycad glycosides is provided in Table 6.

For the several cycad glycosides shown in Table 6, reciprocal inter-conversion through chemical or enzymatic transformation and cleavage has been demonstrated. This is of interest not only because it shows a structural correlation among the glycosides, but also because it suggests a common biosynthetic pathway of the glycosides in the sundry species. The aglycone contains linked nitrogen atoms common to all cycad glycosides and not previously found in a natural product. On acid or enzymatic hydrolysis of the glycosidic bond, the aglycone, which is unstable and not capable of independent existence, decomposes spontaneously to produce nitrogen, methanol, and formaldehyde. On alkaline hydrolysis, a more complex reaction is produced. In addition to nitrogen,

TABLE 6
CYCAD GLYCOSIDES
(1903 - 1960)

CYCAD Genus, Species	Part of Plant	Glycoside*	Sugar	Formula and Melting Point (decomp.)	Reference
1. <i>C. circ.</i>	seeds	pakoecin			Van Dongen, 1903 (168)
2. <i>M. spir.</i>	seeds	macrozamin		$\text{C}_6\text{H}_{11}\text{O}_5\text{N}$ or $\text{C}_6\text{H}_{13}\text{O}_5\text{N}$ m.p. 199°C.	Cooper, 1941 (198)
3. <i>M. reid</i>	seeds	macrozamin*	primeverose	$\text{C}_{13}\text{H}_{24}\text{O}_{11}\text{N}_2$ m.p. 199-200°C.	Lythgoe, 1949 (202)
4. <i>C. rev.</i>	seeds	cycasin	glucose	$\text{C}_8\text{H}_{16}\text{O}_7\text{N}_2$ m.p. 144-145°C.	Nishida, 1955 (212)
5. <i>C. rev.</i>	stem	cycasin			Nishida, 1956 (214)
6. <i>C. circ.</i>	seeds	cycasin	glucose	$\text{C}_8\text{H}_{16}\text{O}_7\text{N}_2$ m.p. 154°C.	Riggs, 1956 (218)
7. <i>C. rev.</i>	male cone	cycasin	glucose		Numata, 1961 (233)

*Except for pakoecin, about which little is known, the common aglycone is $\text{CH}_3\text{N}:\text{N}(\text{O})\text{CH}_2\text{O}$.

**Isolated from *C. media*, *B. ser.*, *M. Miq.* and *E. bark.* by Riggs, 1954 (210).

the reaction yields formic acid, cyanide ion, traces of methylamine, and ammonia (222).

Besides the glycosides, several other constituents of the cycad have been identified. According to Nishida, Yoshimura, in 1922, isolated and identified inositol from the seeds of *Cycas revoluta* (181). In 1949, working on *Macrozamia reidleyi*, Riggs described the isolation and identification of sequoyitol, a monomethyl ether of meso-inositol. One reason for interest in the study of sequoyitol is the high content of inositol normally found in brain and nervous tissues (203).

Animal Research

Banks, in 1770, reported what represents probably the first feeding experiment with cycads (161). After members of his party had become violently ill from eating cycad nuts, they decided to test them on their hogs. Banks wrote: "... the hogs ate them ... and for some time we thought without suffering any inconvenience, but in about a week they were so much disordered that two of them died, and the rest were recovered with great difficulty." Since Banks' time, various kinds of feeding experiments have been made in many areas of the world in an effort to ascertain the toxicity of different parts of the cycad.

Of the 200 or more animal feeding tests with cycads reported in the literature, less than 50 contain sufficient information for the calculation of dose per unit of body weight. Data from 41 feeding experiments have been compiled in Table 7. Seeds, leaves and glycosides were used. Seeds were from two genera, *Encephalartos* and *Macrozamia*; leaves, from *Cycas media* and three species of *Macrozamia*; and glycosides, from *Cycas* and *Macrozamia*. Farm animals included cattle, sheep and pigs; the smaller laboratory animals were rabbits, guinea pigs, rats, mice and frogs. Dosage, mortality and observed signs are given for each feeding test. The toxic effects, both acute and chronic, are discussed as they relate to dose and part of plant.

Acute illness. The illness which follows soon after the ingestion of cycad plant material is characterized by gastrointestinal disturbances. With the fresh kernel of *En-*

cephalartos horridus, an acute condition terminating fatally within hours was produced in rabbits with single test doses of 5.6 or more g/kg (No. 1). Doses of this material given over a longer period produced death within a few days (Nos. 2 and 3). The fresh kernel of *Encephalartos lehmannii* produced a similar condition (Nos. 6 and 7). Fresh kernels of *Macrozamia spiralis* in a single dose of 13.3 g/kg caused death of a sheep within two days (No. 11). With boiled seeds, death occurred within four days (No. 12). The same symptoms, but milder, resulted from a smaller dose of 3.3 g/kg (No. 10). With the feeding of fresh leaves from *Macrozamia pauli guiljelmi*, an acute condition terminating fatally was produced in two heifers (Nos. 15 and 16). The average daily feedings given to the heifers were small when compared with those given to rabbits and sheep (2 g/kg compared with 6 and 13 g/kg). However, the feeding period for the heifers was a month compared with a day for rabbits and sheep. Oral administration of glycosides extracted from kernels of *Cycas revoluta* or *Macrozamia spiralis* produced death in mice within hours with a single dose of 3 mg/g; in guinea pigs, with 1 g/kg (Nos. 33 and 41).

Signs observed in animals with the acute condition appear to be independent of the species of either animal or plant and of the portion of the plant. In the order of their appearance, the most common signs include anorexia, elevated temperature, bloody diarrhea, fecal impaction and respiratory distress. If the animal survives longer than a few days, icterus develops. Death is usually due to respiratory paralysis. Other signs have also been observed with the acute condition. In sheep, Seddon noted rapid twitching of the eyelids, nostrils, lips and jaw muscles, with muscular tremors periodically affecting the entire body (133). Turner also observed muscle twitching in a heifer (137). Hall noted impaired vision in one heifer and photophobia in another (Nos. 16 and 15) (117). Cooper reported inflamed and watery eyes in a guinea pig (No. 41) (198). Seddon reported that sheep were sensitive to light. In several of the feeding tests, animals died suddenly, and no signs were recorded (133).

Pathological findings for the acute condition confirm a diagnosis of gastroenteritis

TABLE 7

FEEDING EXPERIMENTS WITH CYCAD PLANT MATERIAL: KERNEL												
No.	Plant	Preparation	Host	Dosage						Results		Ref.
				Supplement	Route	Frequency	No. Doses	gms/kg*	Duration exp. (days)	No. surv./total	Observed Signs	
1	<i>E. hor.</i>	Fresh	Rabbit	0	p.o.	q.d.	1	5.6	<1	0/1	Anorexia, dyspnea	139
2	<i>E. hor.</i>	Fresh	Rabbit	0	p.o.	q.d.	3	3.3	5	0/1		139
3	<i>E. hor.</i>	Fresh	Rabbit	0	p.o.	q.d.	3	8.6	<4	0/1	Anorexia, apathy	139
4	<i>E. hor.</i>	Outer flesh	Rabbit	0	p.o.	q.d.	11	11.4	11	1/1	Negative	139
5	<i>E. leh.</i>	Outer flesh	Rabbit	0	p.o.	q.d.	7	15.9	7	1/1	Negative	140
6	<i>E. leh.</i>	Fresh	Rabbit	0	p.o.	q.d.	3	6.3	3	0/1	Anorexia, dyspnea	140
7	<i>E. leh.</i>	Fresh	Rabbit	0	p.o.	q.d.	1	18.9	<1	0/1		140
8	<i>M. spir.</i>	Fresh	Pig	0	p.o.	q.d.	5	0.1	5	1/1	Negative	133
9	<i>M. spir.</i>	Fresh	Pig	0	p.o.	q.d.	8	0.5	8	1/1	Negative	133
10	<i>M. spir.</i>	Fresh	Sheep	0	p.o.	q.d.	1	3.3	28	1/1	Anorexia, bloody diarrhea	133
11	<i>M. spir.</i>	Fresh	Sheep	0	p.o.	q.d.	1	13.3	<2	0/2		133
12	<i>M. spir.</i>	Boiled	Sheep	0	p.o.	q.d.	1	13.3	4	0/2	Bloody diarrhea	133

* Daily average grams of plant material per kilogram of body weight.

with moderate to severe liver damage.* Nishida summarized observations on guinea pigs as “. . . macroscopic stagnation and

*With the feeding of fresh kernels of *E. lehmannii* or *E. horridus* to rabbits, Steyn reports as follows: “. . . anorexia, diarrhea, apathy and general icterus was absent.

Post-Mortem Appearances

“General icterus; hydrothorax; hydroperitoneum; hyperaemia and oedema of the lungs with petechiae throughout the lung tissue; congestion of the gastrointestinal mucosa; myocardial haemorrhages; pronounced degenerative and fatty changes in the heart and liver; pronounced congestion of the spleen.

“There were myocardial petechiae, fatty degeneration of the myocardium and an incipient focal myocarditis; pronounced congestion of the lungs and a desquamative bronchial catarrh in an early stage; central and sublobular hepatitis and a perilobular interstitial hepatitis associated with fatty degeneration; pronounced congestion of the spleen; and fatty degeneration of the epithelium of the tubuli contorti.” (135)

bleeding in the lungs, dysfunction of the liver, histological changes in the lung tissue and regressive degeneration of the spleen, kidney, and adrenal glands.” (215). Findings in cattle have been similar to those observed in smaller animals. Liver lesions with necrosis and destruction of the parenchyma, necrotic areas in the mucosa of the abomasum, and acute congestion of the lungs have been reported.*

*Hall has described findings in a 9-month-old heifer weighing about 350 pounds and in good condition at the start of the experiment. The animal was sacrificed on the 29th day after consuming 4 pounds of fresh leaves of *M. pauli guilielmi* within a period of 6 days (Table 7, No. 15). His report is as follows:

“The subcutaneous tissue and visceral fat were oedematous and many petechiae were present. The liver was swollen, yellow, hard to cut and apparently fibrosed. Microscopic examination of sections showed an advanced portal cirrhosis and some centrilobular fibrosis. Liver cells were recognizable as such, but most were vacuolated. The mucosa of the

TABLE 7 (continued)
 FEEDING EXPERIMENTS WITH CYCAD PLANT MATERIAL: LEAVES

No.	Plant	Preparation	Host	Dosage						Results		Ref.***
				Supplement	Route	Frequency	No. Doses	gms/kg	Duration exp. (days)	No. surv./tot.	Observed Signs	
13	<i>M. paul.</i>	P. Dry**	Heifer	Lucerne	p.o.	q.d.	80	1.8	80	1/1	Negative	
14	<i>M. paul.</i>	P. Dry	Heifer	Lucerne	p.o.	q.d.	120	1.4	120	1/1	Calved	
15	<i>M. paul.</i>	Fresh	Heifer	Lucerne	p.o.	q.d.	6	1.9	29	0/1	normally on day 66, Negative	
16	<i>M. paul.</i>	Fresh	Heifer	Lucerne	p.o.	q.d.	6	2.1	28	0/1	Ataxia on day 21 photophobia on day 29	
17	<i>M. paul.</i>	Dry	Heifer	Lucerne	p.o.	q.d.	13	2.9	13	1/1	Anorexia, weakness, pyrexia, impaired vision	
18	<i>M. spir.</i>	P. Dry	Steer	Lucerne	p.o.	q.d.	89	1.1	110	1/1	Negative	
19	<i>M. spir.</i>	P. Dry	Steer	Lucerne	p.o.	q.d.	114	0.5	114	1/1	Ataxia on day 87	
20	<i>M. spp.*</i>	P. Dry	Steer	Lucerne	p.o.	q.d.	35	0.6	35	1/1	Negative	
21	<i>M. paul.</i>	Fresh	Steer	Lucerne	p.o.	q.d.	10	1.4	10	1/1	Negative	
22	<i>M. spir.</i>	Dry	Steer	Lucerne	p.o.	q.d.	103	1.1	103+	1/1	Negative	
23	<i>M. spp.*</i>	P. Dry	Steer	Lucerne	p.o.	q.d.	45	1.2	730	1/1	Ataxia on day 50	
24	<i>M. spir.</i>	P. Dry	Steer	Lucerne	p.o.	q.d.	34	1.3	48	1/1	Ataxia on day 30	
25	<i>M. paul.</i>	Fresh	Steer	Lucerne	p.o.	q.d.	100	2.4	100	1/1	Mild ataxia on day 86. Marked by day 100	
26	<i>M. paul.</i>	Dry	Steer	Lucerne	p.o.	q.d.	22	2.8	22	1/1	Negative	
27	<i>C. media</i>	Fresh	Steer	Bush hay	p.o.	q.d.	13	9.9	42	1/1	Ataxia on day 26	
28	<i>C. media</i>	Fresh	Steer	Bush hay	p.o.	q.d.	16	8.9	59	1/1	Negative	

*mixture *M. doug.* and *M. spir.*

**Partly dry

***13-26 Ref. 117

27-28 Ref. 113

In 10 of the 41 experiments reported in Table 7, an acute condition was produced in five different animal species. These experiments were very oedematous. Microscopic examination of sections showed that most of the epithelial cells had lost their nuclei and the cell walls were ragged in appearance. The blood serum was stained a deep yellow, apparently with bile pigment." (117)

ments, which are summarized in Table 8, show that a number of variables are operating. The limited data do not permit comparison of the relative toxicity of the seeds, leaves and glycosides.

Chronic illness. The predominant signs of chronic illness are locomotor difficulties. These are reported to occur only with the

TABLE 7 (continued)
FEEDING EXPERIMENTS WITH CYCAD PLANT MATERIAL: GLYCOSIDE FROM KERNEL

No.	Plant	Preparation	Host	Dosage					Duration exp. (days)	No. surv./tot.	Results	Ref. ⁵
				Supplement	Route	Frequency	No. Doses	gms/kg				
29	<i>C. rev.</i>	Cycasin	Frogs	Rice	p.o.	q.d.	1	5 mg/g	1	5/5	Negative	
30	<i>C. rev.</i>	Cycasin	Frogs	Saline	s.c. ¹	q.d.	1	3 mg/g	1	5/5	Negative	
31	<i>C. rev.</i>	Cycasin	Mice	Saline	p.o.	q.d.	1	1 mg/g	2	5/5	Negative	
32	<i>C. rev.</i>	Cycasin	Mice	Saline	p.o.	q.d.	1	2 mg/g	2	1/6	Roughened hair, anorexia, apathy, respiratory distress	
33	<i>C. rev.</i>	Cycasin	Mice	Saline	p.o.	q.d.	1	3 mg/g	< (2)	0/6	" " "	
34	<i>C. rev.</i>	Cycasin	Mice	Saline	s.c. ²	q.d.	1	3 mg/g	2	all/all	Negative	
35	<i>C. rev.</i>	Cycasin	Mice	Saline	i.v. ³	q.d.	1	3 mg/g	2	all/all	Negative	
36	<i>C. rev.</i>	Cycasin	Guinea pigs	Saline	s.c. ²	q.d.	1	0.5	2	all/all	Negative	
37	<i>C. rev.</i>	Cycasin	Guinea pigs	Saline	s.c. ²	q.d.	1	1.0	< 2	all/all	Motor inactivity, slight anorexia	
38	<i>C. rev.</i>	Cycasin	Guinea pigs	Saline	p.o.	q.d.	1	0.5	1	all/all	" " "	
39	<i>C. rev.</i>	Cycasin	Guinea pigs	Saline	p.o.	q.d.	1	1.0	2	0/all	Anorexia, atonic paralysis of hind legs in 20 hrs., resp. distress	
40	<i>M. spir.</i>	Macro-zamin	Guinea pigs	Water	s.c.	q.d.	1	1.0	1	all/all		
41	<i>M. spir.</i>	Macro-zamin	Guinea pigs	Water	p.o.	q.d.	1	1.0	< 1	0/all	"Strychnine-like fits" in 1 animal, marked congestion of lungs, eyes swollen, watery and red	

¹ or vehicle

² Thoracic lymph duct

³ on back

⁴ Tail vein

⁵ 29-39 Ref. 215

40-41 Ref. 198

feeding of leaves.* Cattle are most frequently afflicted. One account describes paralysis in a sheep.**

*Nishida has described motor inactivity and an atonic inactivity evident in a guinea pig within 20 hours following administration of cycasin (Table 7, No. 39).

" . . . In the cases administered 1.0 g/kg of Cycasin, motor inactivity and loss of appetite appeared about 14 hours after inocula-

tion into the stomach, and the animals stood quietly in a corner of the experimental cage. In these cases they ran normally after stimulation, but exhaustion with atonic paralysis of the hind legs and dysbasia appeared gradually after about 20 hours. The hair became slightly rough, appetite decreased, and a 2-3°C. decrease in rectal temperature was found. After these symptoms, difficulty in breathing appeared and became stronger with time, and stridor and hoarseness were heard. Moreover, clonic spasm of the entire body,

Appearance and course of the cycad paralysis in cattle have a characteristic pattern. The paralysis is progressive and irreversible. Death occurs when the animal can no longer move about to obtain food and water. Hall suggests that the locomotor difficulties are: "... essentially those of uncontrolled extension and flexion of the hind limbs. This causes dropping of the hind quarters, which may swing to either side. In the early stages there is overextension of the lower hind limbs, and a 'goose-stepping' gait. Later there is incomplete extension, and the beast 'knuckles over' on its phalanges. Affected animals become worse when exercised, and very severe cases will fall with the hind legs extended behind them, dragging themselves along with their forelimbs which are apparently never affected." (116). Increased sensitivity over hind quarters and hind legs was noted in one animal (Table 7, No. 24). With progress of the paralysis, the fetlock joints of the hind legs may enlarge. Horns frequently droop symmetrically and fall off as their connection with skin and horn core become too weak to support them. Muzzle peeling is reported (Table 7, No. 15). Edwards wrote: "... The coat stares; the skin covering the ears, particularly at their tips, becomes bare, and the tips themselves have a tendency to curl, just as in the case of poisoning by ergot of rye. . . The hair loosens

bilateral congestion of the upper bulbar conjunctivae, marked decrease in the respiratory rate (1-2 times per minute) and hiccough were observed. These symptoms became stronger thereafter; there was especially marked clonic spasm of the entire body and agony-like symptoms also appeared. Twenty-four hours later, remarkably bloodshot bulbar conjunctivae and petechiae were seen. The respiratory rate decreased more, and breathing became shallow. The spasm of the entire body disappeared at this time, and respiratory paralysis caused death. . . ." (215)

**Forty-eight pounds of leaves of *M. reidleyi* were fed in 13 weeks. The first signs of paralysis appeared in the hind legs at six weeks; four weeks later, the animal was unable to rise and thereafter developed a complete posterior paralysis. At autopsy "... microscopic examination revealed a demyelination of the spinal cord with a destruction similar to that in the case of lambs affected with copper deficiency (enzootic ataxia) . . ." (114). This feeding test is not included in Table 7 because of the lack of quantitative data.

TABLE 8
CYCADS: FEEDING EXPERIMENTS (TABLE 7) PRODUCING AN ACUTE CONDITION

Feeding Tests (from Table 7)	Nos. 1, 2, 3, 6, 7	Nos. 10, 11, 12	Nos. 15, 16	Nos. 32, 33	Nos. 37, 38, 39, 41
Animal Genus, Species	Rabbit <i>E. hor.</i> and <i>E. leh.</i>	Sheep <i>M. spr.</i>	Cattle <i>M. paul.</i>	Mice	Guinea Pig
Part	Kernel	Kernel	Fresh leaves	<i>C. rev.</i> Cycasin	<i>M. spir.</i> and <i>C. rev.</i> Macroamin, Cycasin
Daily Dosage	3.3-18.9 g/kg	3.3-13.3 g/kg	1.9-21 g/kg	2.0-3.0 mg/g	0.5-1.0 g/kg
No. of Doses	One to three	One	Six	One	One
Total Dosage (g)	5.6-25.8	3.3-13.3	11.4-12.6	No information	No information
Duration of Experiment	One to five days	Two to 28 days	28 and 29 days	One to two days	One to two days

TABLE 9
CYCADS: FEEDING EXPERIMENTS (TABLE 7) PRODUCING PARALYSIS IN CATTLE

Feeding Test (from Table 7)	No. 15	No. 18	No. 23	No. 24	No. 25	No. 27
Sex	Heifer	Steer	Steer	Steer	Steer	Steer
Leaves from <i>Macrozamia</i>	"Fresh"	"Partly dry"	"Partly dry"	"Partly dry"	"Fresh"	"Fresh"
Daily Dosage (g/kg)	1.9	1.1	1.2	1.3	2.4	9.9
No. of Doses	6	89	45	34	100	13
Total Amount (g)	11.4	97.9	54.0	44.2	240.0	128.7
Day Ataxia Noted	21st	87th	50th	30th	86th	26th
Duration of Experiment	29	110	730	48	100	42

over the whole body. . . The tips of the ears are cold. . ." (112).

Pathological studies have contributed little to an understanding of cycad paralysis. At autopsy, muscles of the hind quarters show marked atrophy and are pale with evidence of hemorrhage. Armstrong's observation of spinal cord demyelination suggested a condition similar to that seen in lambs affected with copper deficiency (114). Hall's studies of at least five animals with locomotor difficulties revealed no lesion to explain the paralysis* (117). Edwards reported that examination of the spinal cord showed that "the portion posterior to the middle of the loins had undergone 'white softening'" (112). Hare also noted that the spinal cord of the lumbar and sacral regions appeared pale and softened (118). Except for the above observations, no other reports were found to suggest a neurological basis for the paralysis.

In six of the 41 experiments reported in Table 7, paralysis was produced in cattle following the feeding of leaves of two species of *Macrozamia* and one of *Cycas*. These six cases are summarized in Table 9. As in the acute cases, the limited data do not permit consideration of differences in individual susceptibility and the toxicity of different rations.

Negative findings. No ill effects were recorded for approximately one half of the tests shown in Table 7. Even in large amounts (11 and 16 g/kg), the outer flesh surrounding the pit and stone of seeds of *Encephala-*

lartos had no toxic effect on rabbits (Nos. 4 and 5). The amounts ingested by two pigs were small (less than 1 g/kg) compared with those which were toxic to other animals (Nos. 8 and 9). Cold-blooded animals (frogs, No. 29) were not affected by the glycoside, cycasin, in an oral dose similar to that found to be toxic to mice and guinea pigs. Cycasin caused no permanent ill effects when injected into the tail vein of mice, the thoracic lymph duct of frogs, and the back of mice and guinea pigs (Nos. 30 and 34-37).

Negative findings can be related to the portion of the plant, the dosage, and the animal species. Nishida noted that toxic effects appearing in animals 12 hours or more after oral administration of cycasin are due to the action of digestive or intestinal enzymes. He suggested that toxic effects do not appear following intravenous or subcutaneous injections, because there is probably little or no decomposition of cycasin in either the blood or tissue. Nishida found also that the effects of cycasin on respiration, blood pressure, the heart and blood vessels and on intestinal and isolated tissue preparations were generally slight and showed no increase with higher dosage (215).

Conclusions and Recommendations

This review of the literature of cycads leaves little doubt that many species of this family contain ingredient(s) which is/are toxic to man and animals. Where the plants are indigenous, residents have long been aware of the danger in using cycads for food. Through years of experience, they have developed methods of preparation which have made the cycad a valued food resource. Serious stock losses attributed to consump-

* Spinal cord and brain sections were stained with haemotoxylin and eosin, and additional spinal cord sections, by the Marchi technique (117).

tion of the cycad by cattle have led to bold and expensive efforts to eradicate cycads from grazing areas.

Evidence of the toxicity of cycads comes from many sources. Consumption of the plant or of plant products is reputed to be responsible for various illnesses of man and animals. A variety of minor and vague complaints of humans has been associated with their use. Severe and acute illnesses have been directly related to their consumption. Unfortunately, clinical and laboratory data concerning these ailments are practically non-existent. In animals, two distinct ill effects may occur: acute gastrointestinal disturbances, and a progressive and irreversible paralysis. Each of the conditions has been produced in experiments with selected animal species. Pathological findings for the acute condition show extensive liver damage and mild to severe congestion of other organs and tissues. Pathological studies have contributed little to account for the paralysis in animals. Folk lore attributes a variety of medicinal uses to the plant, many of which are compatible with the presence of a physiologically active ingredient. Recent chemical analyses confirm the presence of a toxic glycoside in several species and genera. Experiments have demonstrated that the glycoside

produces liver damage in laboratory animals, but there is no evidence to relate the paralysis to any specific components of the plant.

Both field observations and results of laboratory experiments show disparity in their findings. Inconsistencies have been related to numerous variables which appear to influence the toxicity of the plant: genera, species, locale, season, maturity and the part of the plant. Consequently, there is need for research in many areas. Chemical investigations should be directed to the search for the toxic components responsible for the production of paralysis in animals. More study is needed on the properties of the glycosides already isolated. It is important to establish reasons for the variation in toxicity of different samples of cycad plant material. Animal research should be expanded in the study of the physiological effects of the cycad and its toxic components on various animal species. In epidemiological investigations, it is important to extend study of the preparation of cycad foods in different localities in order to ascertain the safety of the products for long-term consumption. In areas where cycads are used as food and medicine, efforts should be intensified to determine morbidity and mortality rates for human ailments which might be associated with the use of the plant.

APPENDIX A

Key to the genera of cycads*

A. Leaves twice-divided	<i>Bowenia</i>
A. Leaves once-divided	<i>B</i>
B. Leaflets with distinct mid-vein	<i>C</i>
C. Leaflets with distinct side veins projecting from mid-vein	<i>Stangeria</i>
C. Leaflets with only the mid-vein evident	<i>Cycas</i>
B. Leaflets without distinct mid-vein	<i>D</i>
D. Leaflets widened at point of attachment to rachis	<i>E</i>
E. Leaflets broadest at point of attachment	<i>Dioon</i>
E. Leaflets broadest above point of attachment	<i>Encephalartos</i>
D. Leaflets narrowed at point of attachment	<i>F</i>
F. Leaflets with light-colored swollen area at base	<i>Macrozamia</i>
F. Leaflets without obvious swollen area at base	<i>G</i>
G. Leaflets gradually reduced to two rows of spines near base of leaf	<i>Encephalartos</i>
G. Leaflets not gradually reduced to two rows of spines at base of leaf, but leaf stalks sometimes bearing small scattered spines	<i>H</i>
H. Petiole with scattered spines near base	<i>I</i>
I. Spines $\frac{1}{4}$ - $\frac{1}{2}$ in. long	<i>Ceratozamia</i>
I. Spines about $\frac{1}{12}$ in. long	<i>Zamia loddigesii</i>
H. Petiole without spines	<i>J</i>
J. Stem almost completely underground; leaflets blunt at tip	<i>Zamia</i>
J. Stem aerial with a single trunk; leaflets pointed at tip	<i>Microcycas</i>

* From Missouri Botanical Garden Bulletin. May, 1955, page 80 (98).
Used with permission of R. Tryon.

APPENDIX B
VERNACULAR TERMS FOR CYCADS

Genus	Area	Vernacular
<i>Bowenia</i>	Australia	baio, byfield fern, fern nuts, gun yoo, jul bin, ktg moon ah, ricket fern, <i>Zamia</i> fern
<i>Ceratozamia</i>	Central America	costilla de leon, horned <i>zamia</i> , palma
<i>Cycas</i>	Guam	fadang, federico
	Yap	fallutier, faltar, faltir, fratel, fretel
	Palau	rumi yan
	Nukuoro	manu ata papo
	Fiji	rora, tua wa wa nie
	Australia	bun jinoo, kimalo, nagwiama, <i>Zamia</i> palm
	Indonesia	pakis adji, pakis laut, hindoo-varen
	Malaya	puku gala, todda maram
	India	madan akamapu, wara guda
	Thailand	prong
	Burma	mu dang
	Indochina and China.....	phong nhi thao, prong te koe, tiek chieu, wu lou tzu, su tieh, hai-te-koe, feng wai tsaio
	Japan	sotetsu, tessio
	Ryukyus Islands	nari, yanabu
	Philippine Islands	bitogo, oliva, pitogo
<i>Dioõn</i>	Mexico	cabeza de chamal, chamal, coyolillo, jango, palma de dolores, palma de la virgen, palma de macetas, sotol (?), tio tamal
	Honduras	teo sinte
<i>Encephalartos</i>	Africa	bears' nuts, brood boom, caffre bread, ghost's palm, hosannah palm, hottentot's head, kaffir bread, kpaidei atah, mam pon mere, mod jajes, nm cusa, wild date
<i>Macrozamia</i>	Australia	arumba, banga, baven, burrawang, kammama, mara, nijar, palm, tehalli, wild pineapple, <i>zamia</i> seeds: baio, boyar, byyu, black fellows' potatoes, channing nut, kangaroo nut
<i>Microcycas</i>	Cuba	palma corcho
<i>Stangeria</i>	Madagascar	batsimi saraka, faho, fato, fatra, fatzon, faux sagou tier, samble, tsambou, voa fako, vofaho
<i>Zamia</i>	Florida	coontie, koontie
	Dominican Rep.	guayiga
	Jamaica	sato
	Cuba	palma aleenfor, palma sagu, yuquilla (de raton)
	Puerto Rico	acesiva, malunguey
	Ecuador	Palma de goma

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