

ETHNOBOTANICAL AND PHYTOCHEMICAL INVESTIGATION OF *RANDIA ECHINOCARPA* (RUBIACEAE)*

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RESUMEN

Los frutos de "granjel," *Randia echinocarpa*, se emplean comúnmente en el tratamiento de afecciones renales. Para esta especie no se ha encontrado una larga tradición en la herbolaria mexicana. Es probablemente una aportación reciente de México central. Se realizó un estudio fitoquímico y se extrajeron de los frutos manitol, β -sitosterol y ácidos quinóvico, oxoquinóvico, ursólico y oleanólico. El contenido de triterpenoides de esta especie es consistente con el perfil químico del género *Randia* y géneros relacionados. De las sustancias químicas aisladas, solamente el manitol es un osmodiurético; sin embargo, su presencia no explica las propiedades diuréticas atribuidas al "granjel" en la medicina tradicional mexicana.

Palabras clave: *Randia echinocarpa*, Rubiaceae, planta medicinal, manitol, β -sitosterol, ácido quinóvico, ácido oxoquinóvico, ácido ursólico, ácido oleanólico.

ABSTRACT

The fruits of "granjel," *Randia echinocarpa*, are commonly employed in the treatment of kidney ailments in Mexico. The echinate fruits are probably a recent introduction to the Mexican national "herbolaria" and their use most likely originated in central Mexico. Mannitol, β -sitosterol, quinovic, oxoquinovic, ursolic and oleanolic acids were extracted from the fruits and identified. The triterpenoid content of this species is consistent with the chemical profile of the genus *Randia* and related genera. Even though mannitol is an osmotic diuretic, its presence does not explain the therapeutic properties attributed to "granjel" in Mexican popular medicine.

Key words: *Randia echinocarpa*, Rubiaceae, medicinal plant, mannitol, β -sitosterol, quinovic acid, oxoquinovic acid, ursolic acid, oleanolic acid.

INTRODUCTION

The persistence of medicinal plants in Mexican markets is often considered a testimony to their efficacy and cultural value. This report is a part of a multidisciplinary

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nary program which integrates chemical studies (Reguero *et al.*, 1987) with ethnobotanical investigations (Bye and Linares, 1987; Linares and Bye, 1987) of poorly known yet important Mexican medicinal plants. The Mercado Sonora of Mexico City is the principal national market for herbal remedies. The combination of studying the plants in this central market with subsequent investigations in the source areas of the plants and in various regional and local markets (Bye and Linares, 1983) suggests that certain remedies have been diffused and adopted beyond their original cultural and geographic range. Such plants are most likely to contain substances that produce favorable effects in the curing process.

The fruits of "granjel," *Randia echinocarpa* Sessé et Mociño ex DC., are a conspicuous element of the Mexican "herbolaria" (the collection of mostly plants as well as animals, minerals and articles used in non-institutionalized medical treatments) and are sold beyond the biological range of this species. The fruit, commonly employed in traditional remedies for kidney, pulmonary, circulatory, and gastro-intestinal ailments, was analyzed chemically to see if it contained substances which might explain its alleged therapeutic properties.

Randia echinocarpa is a member of the family Rubiaceae and belongs to the tribe Gardenieae. Synonyms include: *Basanacantha echinocarpa* (Ses. et Moc. ex DC.) Bullock, *Solena echinocarpa* (Ses. et Moc. ex DC.) D. Dietr., and *Genipa echinocarpa* (Ses. et Moc. ex DC.) Gray. It is a member of the subgenus *Basanacantha* (Hook. f.) L. O. Williams., characterized by large flowers and fruits, unisexual flowers, and generally dioecious plants (Williams, 1972).

Randia echinocarpa is a shrub or small tree, 2-6 m high with rigid branches, each short shoot being terminated by four spines. The plant is dioecious but on occasion may be polygamodioecious (Shreve and Wiggins, 1964). The simple, ovate or obovate leaves are opposite and usually evergreen (or drought-deciduous in northwestern Mexico). The solitary flowers are terminal and usually unisexual but sometimes bisexual (Shreve and Wiggins, 1964; Standley, 1926). Pistillate flowers, about 3 cm long, are longer than staminate flowers. The corollas are white, turning orange-yellow with age. The fruits are baccate, subglobose, 4.5-10 cm in



Fig. 1. Immature fruit on shrub near Chimalacatlán, Morelos (Bye & Linares 16038; 30 Aug. 1987).

diameter, covered with irregularly flattened protuberances 0.5-3 cm long, and often yellow when mature. (Fig. 1). The fruits contain numerous, round seeds surrounded by a dark pulp upon maturity. Flowering usually occurs from March to July and fruits mature from July to March.

This species is restricted to the Pacific drainage of Mexico usually growing from near sea level to 1700 m elevation, with most populations occurring between 255 and 1200 m. It ranges from southern Sonora and southwestern Chihuahua to central Guerrero and southwestern Puebla, with the Sonoran Desert marking the northern boundary (Hastings *et al.*, 1972) and the Balsas River drainage forming the southern boundary (Fig. 2). This spiny shrub is usually found in secondary vegetation associated with foothills, hillsides, and flood plains of deciduous tropical, short tree, and thorn forests. Previous reports of its occurrence in Veracruz (Shreve and Wiggins, 1964; Standley, 1926) refer to erroneous label information or mixed labels.

Chemical studies of *Randia* L. *sensu lato* are limited. Previous analyses of plants originally considered members of *Randia* have resulted in the detection, isolation, and structural elucidation of various classes of compounds. Following the current taxonomic concept *Randia sensu stricto*, only neotropical species are considered true members of this genus (D. Lorence, personal communication). Hence, the chemical reports are dominated by paleotropical species that are no longer considered members of *Randia*. These Old World taxa (along with their currently accepted binomials) include: *R. canthioides* Champ. ex Benth. (*Aidia canthioides*) (Champ. ex Benth.) Musamune, *R. dumetorum* (Retz) Poir. in Lam. (*Catunarengam spinosa* (Thunb.) Tirvengadam), *R. formosa* Jacq. (*Rosenbergiodendron formosum* (Jacq.) F. Fagerl.), *R. grandisii* Gamble (no nomenclatural transfer made to date), *R. nilotica* Stapf (no nomenclatural transfer made to date), *R. siamensis* (Lour.) Craib (*Fagerlindia siamensis* (Lour.) Tirvengadam), *R. sinensis* (Lour.) Schult. (*Oxyceros sinensis* Lour.), *R. spinosa* (Thunb.) Poir. (*Catunarengam spinosa* (Thunb.) Tirvengadam), *R. tetrasperma* Benth. et Hook. f. ex Brand. (no nomenclatural transfer made to date), and *R. uliginosa* (Retz) Poir. (*Xeromphis uliginosa* (Retz) Maheshwari). The chemical constituents as originally reported are summarized in Table 1.

Only three species of *Randia sensu stricto* have been investigated prior to our study. Unspecified plant parts of *Randia echinocarpa* yielded arbutin and tannin (Rubio, 1946). Rodríguez (1989) detected oleic and linoleic acids in the fruits and leaves of *R. guerrerensis* Lorence et Rodríguez. Iridoids were isolated from the trunk bark of *R. ruiziana* DC. (Davioud and Bailleul, 1988).

MATERIALS AND METHODS

Ethnobotany. The methodology employed in our market studies (Bye and Linares, 1983) consisted of systematically collecting data and specimens in the Mercado Sonora and other markets, visiting local suppliers, and collecting corroborative specimens and information in the field with herbal collectors. The basic literature on Mexican medicinal plants (Lozoya, 1984) as well as anthropological,



Fig. 2. Distribution of *Randia echinocarpa*. Dots represent localities from which herbarium specimens originated; diagonal lines cover the probable natural range; square indicates the location of the dubious report of the use of this species by Huave Indians of Oaxaca.

ethnobotanical and floristic publications for northwestern and western Mexico were searched for information on *Randia echinocarpa*. Distributional, ecological, and ethnobotanical data were obtained from literature and from specimens deposited in the Herbario Nacional (MEXU) and Facultad de Ciencias (FCME), both located at the Universidad Nacional Autónoma de México (UNAM), after the identity of each was confirmed by R. Bye.

Phytochemistry. The dried fruits used in this study were obtained in the Mercado Sonora, Mexico City, Distrito Federal (Oct. 19, 1986). According to the supplier, these fruits originated near Axochiapan, Morelos (Fig. 3). A voucher specimen (Bye & Linares 15195) has been deposited in the Ethnobotanical Collection of the Jardín Botánico (UNAM). Corroborative herbarium specimens (Bye, 1986) from the source areas (Morelos and Puebla) were also collected (Bye & Linares 15503, 16038, 17023, 17026 MEXU).

Isolated chemical compounds were characterized using three techniques. ^1H Nuclear magnetic resonance (NMR) spectra were recorded on a Varian FT-80 spectrometer in CDCl_3 solutions with TMS as an internal standard. Infrared spectrometry (IR) spectra were taken on a Nicolet FT-IR instrument. Mass spectrometry (MS) spectra were determined at 70 eV using a direct inlet system on a Hewlett-Packard 5985 B spectrometer. Silica gel G (70-230 mesh) was used for column chromatography. Thin layer chromatography (TLC) was done on silica gel 60 G F₂₅₄

TABLE 1
CHEMICAL COMPOSITION OF SPECIES ORIGINALLY REPORT AS MEMBERS OF *RANDIA*
(SEE TEXT FOR CURRENTLY ACCEPTED NAMES)

<i>Species</i>	<i>Plant part</i>	<i>Classes of Chemicals</i>	<i>References</i>
<i>R. canthioides</i>	leaves, stem heartwood, and fruits	sterols	Hui and Ho, 1968
	leaves and stems	β -sitosterol	Hui and Ho, 1968
	stem bark	iridoids	Uesato <i>et al.</i> , 1982
<i>R. dumetorum</i>	bark	triterpene (randialic acids)	Tandon <i>et al.</i> , 1966
	bark, fruit, and seeds	saponins	Atal and Lamba, 1960; Gedeon, 1952; Harkikar and Mohiuddin, 1937; Tandon <i>et al.</i> , 1966
	fruits	mannitol	Anjaneyula <i>et al.</i> , 1965; Kumar, 1965; Tandon <i>et al.</i> , 1966
	fruits	ursolic and oleanolic acids and derivatives	Ansari and Khan, 1981; Kumar, 1965; Hui and Ho, 1968; Saharia and Seshadri, 1980; Woo <i>et al.</i> , 1984; Varshney <i>et al.</i> , 1978
	fruit pulp	essential oil	Harkikar and Mohiuddin, 1937
	leaves	iridoids	Sati <i>et al.</i> , 1986
	leaves, stem heartwood, and fruits	sterols	Joshi <i>et al.</i> , 1981
	seed oil	palmitic, steric, oleic, linoleic, arachidic and lignoceric acids	Ansari and Khan, 1983
	stem bark	coumarins	Tandon <i>et al.</i> , 1966
	<i>R. formosa</i>	stem bark	iridoids
<i>R. grandisii</i>	not specified	ursolic and oleanolic acids and derivatives	Desai <i>et al.</i> , 1970
<i>R. nilotica</i>	stem bark	coumarins	Bashir <i>et al.</i> , 1981
<i>R. siamensis</i>	roots	sterols	Lapikanon <i>et al.</i> , 1983
	roots	ursolic and oleanolic acids and derivatives	Lapikanon <i>et al.</i> , 1983
<i>R. sinensis</i>	leaves, stem heartwood, and fruits	sterols	Hui and Ho, 1968
	leaves and stems	β -sitosterol	Hui and Ho, 1968
<i>R. spinosa</i>	whole plant	triterpene (spinosic acid)	Aplin <i>et al.</i> , 1971
<i>R. tetrasperma</i>	bark, fruit, and seeds	saponins	Quershi and Thakur, 1977
	bark	triterpene (randialic acids)	Quershi and Thakur, 1977
	fruits	mannitol	Quershi and Thakur, 1977
	stem bark	coumarins	Quershi and Thakur, 1977
<i>R. uliginosa</i>	fruits	ursolic and oleanolic acids and derivatives	Ansari and Khan, 1981; Kumar, 1965; Hui and Ho, 1968; Saharia and Seshadri, 1980; Woo <i>et al.</i> , 1984; Varshney <i>et al.</i> , 1978
	not specified	flavonoids	Suxena, 1975; Kumar, 1965
	not specified	tannins	Suxena, 1975; Kumar, 1965

plates (Merck). After development, the plates were sprayed with 1% $\text{Ce}(\text{SO}_4)_2$ in 10% H_2SO_4 and heated. The air-dried, ground fruit (3 kg) was first defatted with hexane. The dried marc was then macerated three times with MeOH. The combined MeOH extracts were concentrated *in vacuo*.

Isolation of Mannitol: The white solid that precipitated spontaneously from the



Fig. 3. Fruits of *Randia echinocarpa* (average diameter of 8 cm). Commercial center near Axochiapan, Morelos, where individual collections are consolidated for commercial wholesale redistribution (26 Oct. 1987).

methanolic extract was purified upon repeated recrystallization from MeOH and compared to the commercial sample of mannitol purchased from Merck.

Fractionation of the Methanolic Extract: After the separation of the mannitol, the remaining methanolic extract was partitioned between EtOAc and water. The resulting organic layer was dried (using Na_2SO_4) and concentrated. The residue was chromatographed in a glass column packed with silica gel (1.5 kg). The initial eluting solvent was CHCl_3 , with the percentage of EtOAc slowly allowed to increase with time. Fractions of 350 ml each were collected.

Isolation of β -sitosterol: Fractions 48-63 eluted with CHCl_3 yielded a crystalline material, which was compared to an authentic sample of β -sitosterol.

Isolation of Quinovic and Oxoquinovic Acids as Their Methyl Ester Derivatives: A white powder was precipitated from fractions 250-312 eluted with CHCl_3 -EtOAc (7.5:2.5). One gram of this material was methylated with CH_2N_2 . The resulting methyl esters were separated into two compounds by preparative TLC developed with CHCl_3 -hexane (9:1).

Oxidation of Dimethyl Quinovate to Dimethyl 3-Oxoquinovate: A solution of 50 g of the first compound in pyridine (1 ml) was added to a well-stirred, ice-cooled suspension of pyridine- CrO_3 complex (prepared from 0.1 g CrO_3 and 1 ml pyridine).

The mixture was stirred for 3 hrs at 0° C, EtOAc (20 ml) added, the supernatant liquid decanted, and the residue washed with EtOAc. The combined EtOAc solution was washed with water, dilute HCl, aqueous NaHSO₃ and water, dried using Na₂SO₄, filtered, and evaporated. The residue (25 mg) was crystallized from MeOH.

Isolation of Ursolic and Oleanolic Acids: The mother liquor left after precipitating the mixture of quinovic and oxoquinovic acids was rechromatographed on silica gel (162 g) using hexane with increasing amounts of CHCl₃. Fractions 34-285, eluted with hexane-CHCl₃ (1:4), afforded a mixture of two additional triterpene acids, which were resolved as previously described (Mata *et al.*, 1988). These acids as well as their methyl ester derivatives were compared to standard reference materials.

RESULTS

Ethnobotany. *Randia echinocarpa* is generally known as "granjel" although other common names (and their variant phonemic transcriptions) are used in separate parts of its biological range (Fig. 4; Table 2). The most common use is medicinal, for which it is widely recognized as a remedy for kidney problems. The detailed information on folk nomenclature and on uses is summarized in Tables 2 and 3, respectively.

In central Mexico, the terms "granjel" and "grangel" are most frequently applied to this plant. "Bola de granjel" and "granjeno chino" are descriptive variants with reference to the rounded fruit with a frizzy surface. The derivation of "granjel" is unknown.

In west-central Mexico, two indigenous names are dominant. "Chacua" and its variants may be Tarascan or Nahuatl in origin.

The Tarascan (= Purépecha) term "xacua" or "shakua" means "quelite" or vegetable (Swadesh, 1969; Velásquez, 1978), while the Nahuatl word "chacual" ('tzacualli') refers to a container used for carrying a ball of an ancient game or to mange (a scalp disease) (Santamaría, 1978). Upon drying, the fruit of *R. echinocarpa* becomes hollow by shrinkage of the seed mass and serves as a container. It is interesting to note that another plant (*Crescentia alata* Kunth), whose dried fruit functions as a container, is called "zacual," a probable phonemic variant of "xacua" and derived from the Nahuatl term 'tzacualli' (cone or deep cup) (Soto, 1987).

The other west-central Mexican native name, "tecoloche" and variants, is Nahuatl in origin, possibly derived from 'tecolhuia' = to blacken and 'octli' = fermented beverage, usually applied to pulque (Siméon, 1984). One variant appears to have "zapol" as the terminating word root which may be derived from 'tzapotl' or the sapote fruit, which has a juicy pulp when ripe that is similar to that of *R. echinocarpa*. One interesting variant from Morelos is "cuahuixcoloctli" ('cuahuix' from 'quauitl' = tree, 'huitz' = spine or 'quaitl' = head; 'coloctli' from 'tecolhuia' = to blacken and 'octli' = fermented beverage). The basic name appears to be derived from the tree's characteristic spines and/or the pulp of the fruit, which tends to blacken and ferment upon maturity.



Fig. 4. Distribution of major common name categories of *Randia echinocarpa*: A = a²ságola; C = crucillo; G = granjel; K = kakáwari; P = papache; T = tecoloche; X = xacua.

Two minor basic names from central Mexico are related to morphological features. "Cirián chino" probably refers to the similarity of the dry, hollow fruit to that of *Crescentia* spp., also known as "cirián" but distinguished by its crinkled surface, hence "chino," a term usually applied to hair with ringlets or curls (Santamaría, 1978). The stem with decussate branches resembles a cross and gives rise to the name "crucillo."

In Chihuahua, Sonora and Sinaloa, the northern part of its range, "papache" and its variants are applied to this plant, although they are used also for other species of *Randia* (Martínez, 1979c). The origin and derivation of this term are unknown. In order to distinguish *R. echinocarpa* from the other species with smooth pericarps, "papache picudo" is used in Sinaloa (Martínez, 1979c). "Papache borracho," referring to the drunken or dizzy effect produced after eating fruits, is said to be a common name for this species in Sonora (R.S. Felger, personal communication); however, published references only apply this common name to other species (Gentry, 1942; Martínez, 1979c). The Tarahumara may have borrowed the lexicon "papache" and modified it to "apache", "apachi," or "apatco." The three ethnic groups of southwestern Chihuahua and adjacent Sonora, Sinaloa, and Durango do not have indigenous terms similar to "papache." The Tarahumara name is "kakáwari" although "batári" (a name applied to fermented drinks) is sometimes used for the bark because it is an additive to "tesgüino" (fermented maize beverage) (Brambila, 1976). The Guarijio call it "a²ságola" which has been

TABLE 2
COMMON NAMES OF *RANDIA ECHINOCARPA* IN MEXICO*

A?SÁGOLA
a?ságola
Chihuahua (Guarijio): Miller, 1978

hosocola
Chihuahua (Guarijio): Gentry in Martínez, 1979a

hosokola
Sonora-Chihuahua (Guarijio): Gentry, 1942

josocola
Chihuahua (Guarijio): Gentry in Martínez, 1979a

GRANJEL
granjel
Distrito Federal, market: *Bye & Linares 11947, 11458, 15195, 16038, 16067, 16068, 16160, 16161*
Guerrero: Cruz, 1979; Martínez, 1969; Rodríguez, 1989;
Fuentes s.n. (MEXU)
México: Martínez, 1979c; *Guízar 1381 (MEXU)*
México, market: Soto, 1978; *Linares & Bye 168*
Morelos: Baytelman, 1979; *Bye & Linares 16038, 17023, 17026*
Puebla: *Téllez et al. 577 (MEXU)*; *Vázquez Rojas 6 (MEXU)*;
Bye & Linares 15503
San Luis Potosí: *Bye & Linares 16221, 16239*
without locality: Gali, 1984; Martínez, 1969

granjel, bola de ...
Distrito Federal, market: Azpiri, 1973; *Bye & Linares 15195*
México: Martínez, 1979b, 1979c
without locality: Gali, 1984

granjel, semilla de ...
México, market: Soto, 1978

grangel
Guerrero: Martínez, 1979a; Soto, 1987, *Riba 198 (FCME)*
Michoacán: Soto, 1987
Morelos: Ortiz, 1986

granjeno chino
Michoacán: Soto, 1987

KAKÁWARI
kakáwari
Chihuahua (Tarahumara): Brambila, 1976

kakwara
Chihuahua (Tarahumara): Pennington, 1963

PAPACHE
apache
Chihuahua (Tarahumara): Mares *et al.*, 1982

apachi
Chihuahua (Tarahumara): Mares *et al.*, 1982; *Bye 1862 (ECON)*, *3348 (ECON, COLO)*, *4001 (COLO)*

apatco
Chihuahua (Tarahumara): Bennett and Zingg, 1935

papache
Chihuahua (Tarahumara; Tepehuan): Gray, 1886; Bennett and Zingg, 1935; Pennington, 1963, 1969; *Bye 1862 (ECON)*, *3348 (ECON, COLO)*, *4001 (COLO)*; *Palmer 1855:A (GH)*

* Collections by Bye and Linares are in the Ethnobotanical Collection of the Jardín Botánico, Universidad Nacional Autónoma de México.

Table 2 continued

- Sinaloa: *Shapiro 279* (MEXU)
 Sonora: *Gentry 2272* (MEXU); Gentry, 1942
 without locality: Martínez, 1969; Standley, 1926
- papache picudo
 Sinaloa: González Ortega in Martínez, 1979a; Martínez, 1969;
 Standley, 1926
- papachi
 Chihuahua: Mares *et al.*, 1982
 Sinaloa: *Kimnach & Sánchez-Mejorada 2036* (MEXU)
 Sonora: Miller, 1978
- TECOLOCHE
- cuahuixcoloctli
 Morelos (Náhuatl): Ortiz, 1986
- tecolochapo
 Guerrero: Martínez, 1979a
- tecoloche
 Guerrero (Náhuatl): Soto, 1987
- tecolonche
 Guerrero: *Riba 198* (FCME)
- tecolosapo
 Guerrero: Reko in Martínez, 1979a; *Montes de Oca s.n.* (FCME)
- tecolozapol
 Guerrero: Hendrichs in Martínez, 1979a
- XACUA
- chacua
 México: Matuda in Martínez, 1979a
 unspecified (Tarasco): Santamaría, 1978
- chacual
 México: Martínez, 1979b
- schacua
 México: *Matuda 27984* (MEXU)
- shacua
 Michoacán: *Soto Núñez, Rico A., Salas N. 21* (MEXU); *Soto Núñez & Martínez Salas 4059* (MEXU); *Soto Núñez 3039* (MEXU); *Soto Núñez 4663* (MEXU)
- shacua
 Michoacán (Tarasco): Soto, 1987
 Guerrero (Tarasco): Soto, 1987
- shaena
 Michoacán: *Martínez Salas & Soto Núñez 1288* (MEXU)
- ticuche
 Michoacán: Cruz, 1979
- xacua
 Guerrero: Reko in Martínez, 1979a
- MISC. NAMES
- batári
 Chihuahua (Tarahumara): Pennington, 1963
- cabeza de negro
 Distrito Federal, market: *Bye & Linares 15195*
- ciriám chino
 México: *Matuda 27984* (MEXU)
- cirián chino
 Michoacán: Martínez, 1979a
- crucillo chino
 Guerrero: Soto, 1987
 Michoacán: Soto, 1987
- crucecillo

Table 2 continued

Guerrero: Herrera, 1986
Morelos: Bonfil & Domínguez 3 (MEXU)
cruceta
Morelos: Cruz, 1979
savóchi
Chihuahua (Tepehuan): Pennington, 1969

transcribed as "hosocola" and its variants (Miller, 1978). The Tepehuan refer to it as "savóchi" (Pennington, 1969).

In most Mexican markets *R. echinocarpa* is known as "granjel" or "bola de granjel." Occasionally the fruit in Mexico City markets is also called "cabeza de negro" because protuberances of the fruit resemble the curly hair of black people.

The most common use of "granjel" is to alleviate various kidney ailments, such as kidney pains, kidney stones, and "bad" urine. Throughout Mexico, the whole fruits are prepared in an infusion or a decoction (1 fruit for 1/4 - 1/2 liter of water; 30g per liter) and consumed as a simple tea three times a day as well as general drinking water ("agua de uso") (Baytelman, 1979; Martínez, 1939, 1969; Bye & Linares 11947, 15195, 16038, 16067, 16160, 16161; Guízar 1381; Soto Núñez 21, 187, 3039, 4663; Vázquez Rojas 6). The commercial herbal diuretics known as "riñozán" and "tisana uva" include "granjel" (Bye & Linares 16160, 16161).

In addition, tea made from the fruit or leaves is drunk to treat coughs, circulation ailments, diabetes, and diarrhea. Older reports mention the consumption of fruit in the treatment of malaria. In general, the "hot-cold quality" (Viesca, 1984) of the fruit "granjel" is considered to be fresh ("fresco").

There are no reliable accounts on the medicinal use of *R. echinocarpa* from the nineteenth century and earlier. Among the wild edible fruits of southwestern Chihuahua reported by the Franciscan missionaries during the eighteenth century were "papachos" at Temoris near Guazapares (Fernández de Lis, 1777) and "papa-chis" at Chínipas (Solórzano, 1777). The publications of the Instituto Médico Nacional, responsible for the testing, standardization, and promotion of herbal medicines in Mexico between 1888 and 1915, did not report this plant (Fernández, 1961; Guerra, 1950). One of the earliest post-conquest botanical references of New Spain, *Historia Natural de Nueva España* by Francisco Hernández, is the most important because it was commissioned specifically to document medicinal plants, recorded the greatest number of plants, and covered a large geographic area, which included the southern range of *R. echinocarpa*. Of the 3,076 plants listed, 1,014 have been determined to a generic or specific rank. To date, *R. echinocarpa* has not been identified in the monumental work of Hernández (Valdés and Flores, 1984).

The first published reference to the medicinal employment was that of Martínez (1939). Its inclusion in contemporary, popular self-medication guides such as that of Gali (1984) suggests subsequent diffusion of "granjel" in the popular medicine of Mexico.

In addition to its medicinal properties, *R. echinocarpa* provides edible fruit pulp, an additive to aid fermentation, and a blue dye and is reportedly employed for hallucinogenic purposes (Table 3). The earliest documentation of its use was made

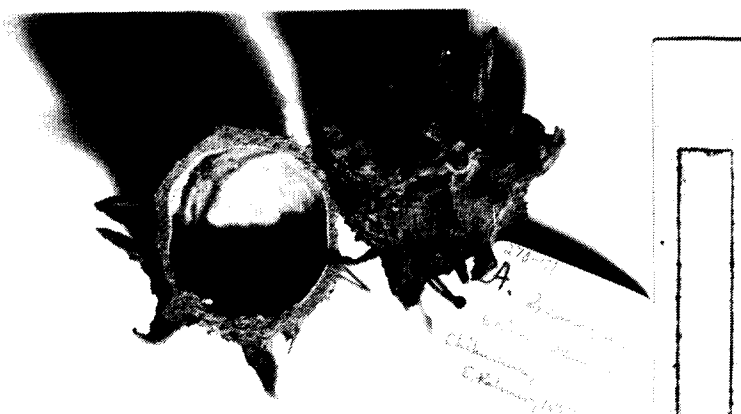


Fig. 5. Ethnobotanical collection of this plant, made by Edward Palmer (1885-A, GH) from the Batopilas area, Chihuahua (August-September, 1885).

by Edward Palmer in 1885 when he collected the fruit (Fig. 5) as a source of food and dye near Batopilas, Chihuahua.

A special note is made about a recent, dubious ethnobotanical record of *R. echinocarpa* from Oaxaca. As can be seen in figure 2, the geographic location of the report of this species used by the Huave Indians is outside of the distribution of this taxon. Zizumbo and Colunga (1982) state that the flowers of "mbaj wajtstats" or "tsats mbaj" ('flor de espinas') are used medicinally. The sterile specimens (Zizumbo et Colunga 60, FCME, MEXU) have been reidentified as *R. tetraantha* (Cav.) DC., a closely related species, which is known to grow in the region (D. Lorence, personal communication). In the future, collections of fruiting specimens should be made to determine the identity of this reported medicinal plant of the Huaves in coastal Oaxaca.

Phytochemistry. The recrystallization of the white powder precipitated from the methanolic extract produced 7.5g (total yield 0.25% dry wt.) of mannitol (melting point (mp) 167° C) which was identical to the commercial sample.

The remaining methanolic extract was partitioned between EtOAc-H₂O. Silica gel chromatography of the resulting organic phase allowed the isolation of β -sitosterol and four triterpene acids, namely, ursolic, oleanolic, quinovic and oxoquinovic acids. Fractions 48-64 from the original column yielded β -sitosterol (total yield 0.005% dry wt.) (mp 137° C) which was identical to the authentic sample. Fractions 250-312 afforded 4g, a mixture of quinovic acid and oxoquinovic acid (Fig. 7). Methylation of 1g of this mixture and subsequent chromatographic separation produced 600mg (total yield 0.08% dry wt.) of dimethyl quinovate (Fig. 6a) and 250 mg (total yield 0.03% dry wt.) of dimethyl oxoquinovate (Fig. 7a.) Dimethyl quinovate, mp 170-171° C (Lit. mp, 163-165° C (Adeoye and Waigh, 1983)); IR ν_{\max} (KBr): 3651, 1720 cm⁻¹; MS m/z (rel. int.): 514 (82), 496 (2), 484 (1), 274 (87), 207 (100), 55 (89); ¹H NMR (δ): 5.6 (t, $J=3$ Hz, H-12), 3.61 (s, 3H, -COOMe), 3.60 (s, 3H, -COOMe), 3.17 (dd, $J=8, 6$ Hz, H-3), 2.25 (d, $J=10$ Hz, H-18), 0.91-0.74 (2d, 4s, 6-Me). Dimethyl 3-oxoquinovate, mp= 145° C, (Lit. mp, 144-145° C (Adeoye and

Waigh, 1983)); IR ν_{\max} (KBr): 1720, 1690 cm^{-1} ; MS m/z (rel. int.): 512 (25), 453 (50), 306 (20), 274 (44), 262 (17), 247 (35), 215 (40), 205 (35), 55 (60), 41 (100); ^1H NMR (δ): 5.6 (t, $J=3$ Hz, H-12), 3.6 (s, 3H, -COOMe), 3.60 (s, 3H, -COOMe), 3.17 (dd, $J=8, 6$ Hz, H-3), 2.25 (d, $J \times 10$ Hz, H-18), 0.91-0.74 (2d, 4s, 6-Me.)

The oxidation of 50 mg of dimethyl quinovate produced 25 mg of a residue (mp 147°C) and was undepressed by admixture with a sample of dimethyl ester of oxoquinovic acid. The IR and ^1H NMR spectra of the two samples were identical.

After the separation of the mixture of quinovic and oxoquinovic acids, fractions 250-312 (8 g) from the original column was rechromatographed. Fractions 34-285 of this column yielded 1.5 g of a mixture of oleanolic and ursolic acids (mp 250°C .) Resolution of 1 g of the mixture yielded ursolic acid (380 mg; total yield 0.017% dry wt.; mp $278-279^\circ\text{C}$) and oleanolic acid (100 mg; total yield 0.005% dry wt.; mp greater than 300°C). Both acids, as well as their methyl ester derivatives, were identical to standard reference materials.

DISCUSSION

Based upon the data available, "granjel" appears to be a recent addition to the Mexican national "herbolaria." Its absence from the recorded herbal remedies until the 1900's and its widely used common name, "granjel," suggest that it was a local remedy in central Mexico (Morelos, Puebla, and adjacent Guerrero) and that it diffused rapidly throughout the country. During the late 1880's and early 1900's, the Instituto Médico Nacional disseminated information about many remedial plants which are popular today (Fernández, 1961). However, in the case of *Randia echinocarpa*, there does not appear to be any scientific study which legitimized and promoted its use. Perhaps the claims of its efficacy circulated through the exchange routes between the central and regional markets, and "granjel" was accepted subsequently by the consumers.

An earlier study (Rubio, 1946) identified arbutin in the fruits of *R. echinocarpa*. This glucopyranoside is an effective diuretic and urinary anti-infective (Windholz, 1983).

Of the six substances isolated from the fruits in this report, only mannitol is reported to have therapeutic activity related to kidney ailments (Windholz, 1983), for which "granjel" is most commonly employed. As an osmotic diuretic, mannitol is extensively used as a prophylaxis for acute renal failure (Weiner and Mudge, 1985.) It increases or maintains high urine volume without an increase of sodium loss (Meyers *et al.*, 1974). Mannitol is water-soluble but is not readily absorbed in the gastrointestinal tract (Tyler *et al.*, 1981). It is usually given intravenously and rarely administered orally. Although the mannitol would be present in the herbal tea, it probably would not have a noticeable effect upon the kidneys due to low yield and poor absorption. Based upon contemporary models that describe the actions of diuretics in relation to kidney disorders, it is difficult to explain chemically any therapeutic effects of *R. echinocarpa*. Pharmacological evaluations of quinovic and oxoquinovic acids and their effects on renal dysfunction are needed.

TABLE 3
USES OF *RANDIA ECHINOCARPA* BY CATEGORIES, PARTS OF THE
PLANT, AND STATE*

DYE (blue dye)

Fruit

- Chihuahua / Gray, 1886; Palmer 1855:A (GH)

EDIBLE FRUIT

(interior pulp surrounding the seeds)

- Chihuahua (Tarahumara; Tepehuan) / Bennett and Zingg, 1935; Gray, 1886; Mares *et al.*, 1982; Pennington, 1963, 1969; Bye 1862 (ECON), 3348 (ECON, COLO), 4001 (COLO); Palmer 1855:A (GH)
- Guerrero / Montes de Oca *s.n.* (FCME)
- Sinaloa (Indians and Mexicans) / Standley, 1926; Martínez, 1969; Palmer 1887:309 (GH); Shapiro 279 (MEXU)
- Sonora-Chihuahua (Guarijio) / Gentry, 1942
- Unlisted locality / G.B. Hinton 4271 (NY); von Reis and Lipp, 1982
- unspecified / Martínez, 1969

FERMENTED BEVERAGE ADDITIVE

Bark: crushed and heated, added to fermenting "tesgüino" mixture of maize (*Zea mays* L.), roasted crowns of maguey (*Agave* spp.), and fruits of "chawé" (*Lemaireocereus thurberi* (Engelm.) Britt. et Rose) and "napihora" (*Cephalocereus leucocephalus* (Poselger) Britt. et Rose)

- Chihuahua (Tarahumara) / Bennett and Zingg, 1935; Pennington, 1963; Bye 3348 (ECON, COLO)

Bark: beverage catalyst

- Chihuahua (Tepehuan) / Pennington, 1969

Bark, seeds: "tesgüino"

- Chihuahua (Tarahumara) / Bye 3348 (ECON, COLO)

HALLUCINOGEN

- Guerrero / Rodríguez, 1989

MEDICINAL USES

Abortifacient

Fruit: eaten

- Guerrero / Herrera, 1986

Cancer of the stomach and intestines

unspecified part

- Distrito Federal, markets / Azpiri, 1973
- Veracruz, markets / Azpiri, 1973
- not specified / Martínez, 1969

Circulatory problems, varicose veins

Fruit: infusion / oral

- Distrito Federal / Bye & Linares 11458
- San Luis Potosí / Bye & Linares 16221

* 1. Fruit refers to whole fruit unless otherwise noted; 2. collections by Bye and Linares are in the Ethnobotanical Collection of the Jardín Botánico, Universidad Nacional Autónoma de México.

Table 3 continued

Coughs

- Fruit: tea / oral
 - Distrito Federal, market / *Bye & Linares 16038*
- Leaves, roots: infusion / oral
 - Morelos / *Bye & Linares 15503*
- Fruit: eaten
 - Morelos / *Bye & Linares 16038*

Diabetes

- Fruit: eaten
 - Sinaloa / *Shapiro 279* (MEXU)
- Fruit, leaves: tea / oral
 - Distrito Federal, market / *Bye & Linares 16067, 16068*
 - Michoacán / Soto, 1987

Diarrhea

- Fruits, leaves: decoction / oral
 - not specified / Gali, 1984; Martínez, 1979b, 1979c
- Leaves: decoction / oral
 - Distrito Federal, markets / Azpiri, 1973
 - Guerrero / Martínez, 1969
 - México, market / Soto, 1978
 - Veracruz, markets / Azpiri, 1973

Hiccup

- Fruit: eaten
 - Sinaloa / *Shapiro 279* (MEXU)

Injuries and wounds caused by accidents or external violence

- Fruit: beverage (with *Crescentia alata* Kunth) / oral
 - Michoacán / Soto, 1987

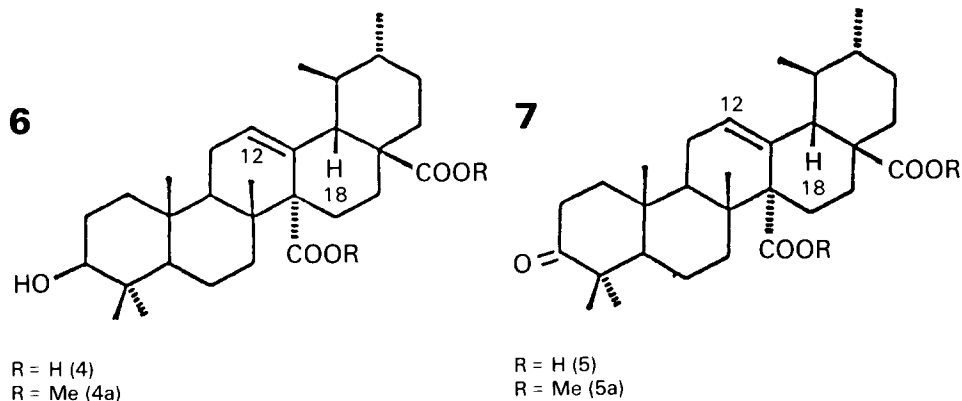
Kidney ailments

general ailments, as diuretic

- Fruit: tea, infusion (with *Selaginella*; with *Selaginella*, *Equisetum*, and *Heterotheca*; with *Serjania* and *Amphipterygium*) / oral
 - Distrito Federal, market / *Bye 17943*
 - México, market / Soto, 1987; *Linares & Bye 168*
- Fruit: tea, infusion / oral
 - Distrito Federal, market / Cruz, 1979; *Bye & Linares 11947, 11458, 15195*
 - Morelos / Ortiz, 1986
 - Morelos, markets / Cruz, 1979
 - Michoacán, markets / Cruz, 1979
 - Puebla / *Guízar 1381* (MEXU)
 - San Luis Potosí / *Bye & Linares 16221*
- Fruit, leaves: tea, decoction (with *Selaginella*) / oral
 - Distrito Federal, market / Azpiri, 1973; *Linares et al.*, 1984; *Bye & Linares 16067, 16068*
- Fruit, leaves: tea, decoction / oral
 - Michoacán / *Soto Núñez 4663* (MEXU)
 - Veracruz, markets / Azpiri, 1973
- Fruit, leaves, root: tea / oral
 - Puebla / *Vázquez Rojas 6* (MEXU)
- Fruit, leaves, stems: infusion / oral
 - Michoacán / Soto, 1987
- Fruit, flowers: infusion (with *Opuntia*) / oral
 - Morelos / *Bye & Linares 17023*
- Leaves: decoction / oral
 - Morelos / Baytelman, 1979
 - Unspecified / Martínez, 1969
- Leaves, roots: infusion / oral
 - Morelos / *Bye & Linares 15503*

Table 3 continued

- unspecified part
 - Guerrero / Rodríguez, 1989
- "bad" urine
 - Fruit: tea / oral
 - Morelos / Ortiz, 1986
 - Leaves: infusion / oral
 - Michoacán / Soto, 1987
 - Fruit: infusion (with *Zea mays* L., *Parmentiera edulis* DC., unidentified palm) / oral
 - Morelos / Ortiz, 1986
 - Fruit: infusion (with *Equisetum* sp.) / oral
 - Distrito Federal, market / Bye 17943
- kidney pains and inflammations
 - Fruit: infusion (with *Equisetum* sp.) / oral
 - Distrito Federal, market / Bye 17943
 - Fruit, leaves: decoction / oral
 - Guerrero / Herrera, 1986
 - Michoacán / Soto Núñez 187 (MEXU), 3039 (MEXU)
 - Leaves, stems: decoction / oral
 - Michoacán Soto Núñez, Rico A., Salas N. 21 (MEXU)
- kidney stones
 - Fruit: infusion / oral
 - Distrito Federal, market / Bye & Linares 15195
- Liver ailments
 - Fruit: infusion (with *Equisetum* sp.) / oral
 - Distrito Federal, market / Bye 17943
- Malaria
 - Fruit: eaten
 - Sinaloa / Palmer 1887:309; Martínez, 1969; Standley, 1926
- Nerves (ailments of nervous system)
 - Fruit: tea / oral
 - Morelos / Ortiz, 1986
- Pain, waist
 - Fruit, leaves: decoction / oral
 - Guerrero / Herrera, 1986
- Respiratory illnesses
 - chest chills, bronchitis, colds
 - Fruit: beverage (with *Crescentia alata* Kunth) / oral
 - Michoacán / Soto, 1987
 - Fruit: (pulp & seeds): eat
 - Morelos / Bye & Linares 17026
 - Seeds: tincture in wine / oral
 - San Luis Potosí / Bye & Linares 16221
- Rheumatism
 - Fruit, leaves: decoction / oral
 - Guerrero / Herrera, 1986
- Stomachic
 - Fruit
 - Chihuahua (Tarahumara) / Brambila, 1976
- Not specified (medicinal)
 - Morelos / Bonfil & Domínguez 3 (MEXU)



Figs. 6-7. Chemical structures. 6. Quinovic acid (3) and dimethyl quinovate (3a). 7. Oxoquinovic acid (4) and dimethyl 3-oxoquinovate (4a).

CONCLUSIONS

The presence of *Randia echinocarpa* in the Mexican "herbolaria" does not appear to have a long tradition, even though the fruits are sold beyond the plant's biogeographic range. The use of the fruits to alleviate kidney ailments and the common name, "granjel," probably diffused from central Mexico during the twentieth century. The triterpenoid content of this species is consistent with the chemical profile so far known for the genus *Randia* and related genera. Of the six substances isolated from the fruits of *R. echinocarpa*, only mannitol is used in treating renal ailments as an osmotic diuretic. However, mannitol is not readily absorbed by the intestines. Therefore, current models and therapeutic practices of allopathic medicine do not explain the rationale for the use of "granjel" in Mexico's popular medicine.

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