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Fitoterapia. Author manuscript; available in PMC 2013 March 1.

Published in final edited form as:
Fitoterapia. 2012 March ; 83(2): 266–271. doi:10.1016/j.fitote.2011.11.018.

The Potential Health Effects of *Melicoccus bijugatus* Jacq. Fruits: Phytochemical, Chemotaxonomic and Ethnobotanical Investigations

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Abstract

Most natural product research is market-driven and thus many plant species are overlooked for their health value due to lack of financial incentives. This may explain the limited information available about the health effects of the edible fruit species *Melicoccus bijugatus*, a member of the Sapindaceae family that grows mostly in the Caribbean and in parts of South America. However, recent phytochemical studies of these fruits have shed some light on their biological effects. In this review the health effects of *M. bijugatus* fruit pulp and seeds are assessed in relation to phytochemical and ethnobotanical studies, as well as chemotaxonomic information and medicinal uses of other Sapindaceae species. The chemistry of *M. bijugatus* fruits was found to be different than the other Sapindaceae fruits, although some of the medicinal uses were similar. Specific phenolics or sugars in *M. bijugatus* fruits may contribute to their therapeutic uses, especially for gastrointestinal problems, and to some extent toxicological effects. This review focuses our understanding about the specific biological effects of *M. bijugatus* fruits, which may be useful for predicting other medicinal uses, potential drug or food interactions and may benefit people where the fruits are prevalent and healthcare resources are scarce.

Keywords

Melicoccus bijugatus; Fruit; Pharmacognosy; Phenolics; Sugars; Sapindaceae

1. Introduction

The edible fruit species *Melicoccus bijugatus* is a minor member of the Sapindaceae family, otherwise known as the Soapberry family [1]. *M. bijugatus* is a woody slow-growing tree believed to have originated in northern South America or more specifically in the regions of Columbia, Venezuela, French Guiana, Guyana, Surinam and the island of Maragarita [2]. *M. bijugatus* is grown and consumed mostly in these regions as well as in Costa Rica, Nicaragua, El Salvador, Panama, and the Caribbean; especially in Puerto Rico, Haiti, Dominican Republic, Cuba and Jamaica. In the continental United States the fruits grow best in Florida, mostly in Key West [2].

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M. bijugatus fruits have green leathery skins covering a fleshy salmon-colored pulp (sarcotesta) that adheres to a crustaceous seed coat containing the embryo [1, 2]. *M. bijugatus* fruits are often found growing wild in backyards, along roadsides and trails in their native regions. Although most fruit trees are grown naturally from seed, some superior cultivars are propagated by air layering or grafting in Puerto Rico and in Florida [2]. *M. bijugatus* fruits ripen in the summer months (usually July to September) [2]. Street vendors, often children, sell these fruits to tourists or locals seeking refreshments in the summer heat [2, 3]. *M. bijugatus* fruits from the Caribbean are also sold seasonally, in limited quantities, at fruit markets in the northeast of the United States, including New York City, Boston and Philadelphia [3].

M. bijugatus fruits are related to several species with more international acclaim: longan (*Dimocarpus longan* Lam.), lychee (*Litchi chinensis* L.) and rambutan (*Nephelium lappaceum* L.) [4]. Unlike their Asian relatives, *M. bijugatus* fruits have been of little horticultural interest over the years and of marginal economic importance [2]. This may be because the fruits are mostly popular in native fruit regions where they have little monetary value. Moreover, the physical characteristics of these fruits may contribute to their limited commercial success in the international market; the pulp is often difficult to separate from the seed and usually only small quantities of edible pulp are obtained after a labor-intensive effort.

Although insufficient financial incentives may explain the lack of research on the health effects of these fruits, there are several ethnomedicinal uses of *M. bijugatus* fruit pulp and seeds reported in literature [2, 3, 5–9]. Much of this information comes from northern South America, but more recent investigations provide information from the Caribbean islands. Information about the potential biological activities of *M. bijugatus* fruits is also obtainable from chemotaxonomic information of other Sapindaceae fruit species. In order to better understand the health effects of this under-researched fruit species, this review provides information about the ethnobotany and phytochemistry of these fruits as well as chemotaxonomic and medicinal uses of other Sapindaceae fruits with more commercial value.

2. Ethnobotanical information

2.1 Seed tissues

Ethnobotanical information about *M. bijugatus* seeds comes mostly from areas where the fruit species originated, namely the Orinoco region, which now encompasses the modern-day countries of Columbia and Venezuela. In Venezuela the roasted seeds are pulverized and mixed with honey and consumed as a syrup or tea to halt diarrhea [2]. The roasted embryo is also prepared and consumed similarly to chestnuts for dietary uses [2]. The indigenous people of the Orinoco region used the cooked seeds as a substitute for cassava, or ground it into a flour to make bread [5]. In Nicaragua, the use of the seed milk or “horchata” is reported to treat parasites [6]. Usually the seeds are roasted before consumption for either dietary or medicinal purposes, most likely to reduce the toxicity of the seeds or make them more digestible.

2.2 Fruit pulp tissues

M. bijugatus fruit pulp is mostly consumed as a food or beverage. The juice from the pulp of the fruit is usually sucked until all that remains is the fibrous material attached to the seed. Pie filling, jam marmalade or jelly is made from the pulp [2]. The peeled fruits are also boiled to make juice for cold drinks and the fruit juice has been used as an experimental dye [2]. In Columbia, the juice has been canned commercially, and in the Vieques Island, Puerto Rico an alcoholic drink known as “bili” is made by aging rum with the fruits [1, 2]. The fruit

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pulp is also used for the treatment of hypertension, asthma, diarrhea and constipation [7–9]. Additional ethnobotanical information, acquired from interviews of people from the Dominican Republic and Cuba, indicated that *M. bijugatus* fruit pulp has possible toxic effects in adolescents [3]. The fruit pulp was also reported to be an irritant to the throat when consumed in large quantities. However, macerating the seeds with the teeth and then sucking the seed juice was reported to alleviate this condition [3].

3. Ethnobotanical comparisons with related species

M. bijugatus fruits have some ethnobotanical uses in common with three other related fruit species that are more commercially available and used in traditional Chinese medicine: *Nephelium lappaceum* L. (Rambutan), *Dimocarpus longan* Lour. (Longan) and *Litchi chinensis* Sonn. (Litchi) [2]. The seeds of both *M. bjugatus* and *L. chinensis* are used for the treatment of intestinal problems [2, 3]. *M. bijugatus*, *D. longan* and *L. chinesis* seeds have all been noted for their use as an astringent [2]. The pulp from *M. bijugatus*, as well as *N. lappaceum*, *D. longan*, *L. chinensis*, are used for dietary purposes and to treat stomach problems [2, 8]. Specifically, the pulp of *M. bijugatus* fruits is used to treat constipation and diarrhea, whereas *D. longan* and *N. lappaceum* pulp are reportedly used to expel parasites, or used as a stomachic to stimulate digestion [2]. Furthermore, the pulp of *L. chinensis* is used for its beneficial effects on stomach ulcers, gastralgia and tumors [2].

Both *M. bijugatus* and *L. chinensis* fruits are also used for treating respiratory problems. *M. bijugatus* pulp was used for “debiles de pecho”, literally translated as “weak chest”, and refers to respiratory difficulties, whereas *L. chinensis* was reportedly used for treating coughs [2, 8]. Based on the ethnobotanical literature, it does not appear that *M. bijugatus* fruits have pain-relieving effects or alkaloid content, unlike the seeds of *L. chinensis* and *N. lappaceum*, which are used as an analgesic [2].

It is also worth noting that the seeds of *D. longan* with the rind of the fruit can be used as shampoo [2]. This is probably due to the detergent-like properties of saponins in these tissues, which are common in the Sapindaceae family [4]. Similar saponins may also be responsible for the piscicidal (fish poison) properties of the closely related species *Talisia squarrosa*, a member of same tribe as *M. bijugatus* fruits (*Meliccoccae*) [10]. Although there are no reports of using *M. bijugatus* fruits as a detergent or as a fish poison, unidentified saponins at lower and less toxic concentrations may be present in these fruits.

4. Phytochemistry: phenolics and sugars

Mass spectrometry and HPLC analysis of *M. bijugatus* fruit tissues indicated the presence of many different types of phenolics (Fig. 1) and their sugar derivatives. In the embryo part of the seed tissues mostly flavonoids were identified including epicatechin, catechin, epigallocatechin, B-type procyanidins (dimers), naringenin, naringenin derivatives, phloretin, phloridzin, quercetin, myricetin and resveratrol [11]. The hydroxycinnamic acid, sinapic acid, was also identified [11].

In the seed coat tissues the flavonoids most prevalent were procyanidins, especially trimers and dimers [11]. This differed from the embryo tissues, which had mostly dimers and monomers [11]. An A-type procyanidin was also identified in seed coat tissues but not in embryo or pulp tissues [11]. A-type procyanidins are structurally different, by one ether bond, than the more common B-type procyanidins, (Fig. 1) and may contribute to unique biological effects of the seed extracts [12]. Additionally, the major phenolic acids identified in the seed coats were coumaric acid derivatives, which were not found in the embryo tissues [11].

In contrast to the seed tissues, there were no epicatechin, catechin, or catechin derivatives identified in the pulp tissues. Most of the phenolics identified in these tissues were phenolic acids, in particular coumaric acid and ferulic acid derivatives [11]. Resveratrol derivatives and a benzyl alcohol derivative were also detected in the pulp, as well as in the embryo and seed coat tissues [11]. Moreover, the HPLC fingerprint profile of the pulp tissues, indicated there was a major unidentified peak detected at 280 nm that is likely to be a phenolic compound [3, 11].

Sugars were also investigated in both the pulp and embryo tissues of several different cultivars of *M. bijugatus* fruits [11, 13]. Sucrose, glucose and fructose were the major sugars detected [11, 13]. These sugars were present in higher amounts in the pulp than the embryo tissues [11, 13]. The ratio of glucose to fructose was approximately 1:1 in fruit pulp and 0.2:1 in the embryo tissues [13]. Sorbitol, raffinose family oligosaccharides, cyclitols or galactosyl cyclitols were not detected. Small amounts of mannose and trace amounts of raffinose were detected in pulp and embryo tissues [11].

5. Chemotaxonomy

Catechin derivatives or condensed tannins were identified in the seeds of *M. bijugatus* and three other species: *Nephelium lappaceum* L., *Dimocarpus longan* Lour. and *Litchi chinensis* Sonn. However, there were no ellagic acid, ellagotannins or hydrolysable tannins detected in *M. bijugatus* seeds or pulp, which were present in the seeds, pulp, and peel of *D. longan*, as well as the peel of *N. lappaceum* [11, 14, 15]. A-type procyanidins were present only in the seeds of *M. bijugatus* and *D. longan* but may be in other tissues in the other species [11, 16, 17]. Anthocyanins were not detected in *M. bijugatus* pulp or seeds but detected in *L. chinensis* pulp [11, 18]. Some quercetin derivatives were present in *M. bijugatus* embryo tissues as well as *L. chinensis* pulp [11, 18]. Interestingly, coumaric acid and coumaric acid derivatives were identified in *M. bijugatus* pulp tissues but do not appear to be in the pulp or embryo tissues of the other three species [14–17]. Both *M. bijugatus* and *N. lappaceum* have very similar ratios of the sugars sucrose, glucose and fructose [19, 11]. In addition several cultivars of *L. chinensis* also had fructose nearly equal to glucose or less than glucose, although the relative amounts of sucrose were different [18].

6. Potential biological effects

6.1 Seeds tissues

The biological activities of phytochemicals identified in the embryo of *M. bijugatus* fruits, and their associated ethnomedicinal uses, are presented in Table 1. Most ethnomedicinal uses of *M. bijugatus* seeds appear to be associated with the treatment of gastrointestinal problems. The crushed seeds, consisting of the embryos and possibly the seed coats are mixed with a syrup or hot water to treat diarrhea [2, 8]. This medicinal effect may be due to epicatechin and the less prevalent catechin and procyanidin B2 found in all parts of the seeds [11]. These compounds inhibit chloride transport by the cystic fibrosis transmembrane conductance regulator (CFTR) in human colon epithelial cells, ranked in the following order: epicatechin > catechin > procyanidin B2 [20]. These phytochemicals prevent dehydration and nutrient loss associated with diarrhea by blocking chloride transport [20]. Catechin derivatives also have antimicrobial activity, which could destroy the microorganisms causing diarrhea [21]. Moreover, A-type procyanidins found in the seed coats, have anti-adherence effects on bacteria and are likely to be in the seed preparations used for treating gastrointestinal problems [22].

The astringency of the embryo tissues, most likely caused by epicatechin, catechin dimers and possibly trimers, are also suggested to control diarrhea by constricting gastrointestinal tissues, which could prevent secretions and nutrient loss [23]. The anti-parasitic activity of the embryo may be due to the presence of the compound naringenin, which is reported to have the most activity against the parasites *Cryptosporidium parvum* and *Encephalitozoon intestinalis* compared to several other flavonoids [24]. The embryo juice may alleviate throat irritation from the pulp by affecting the binding affinity of astringent phenolics from the pulp. Changes in ionic strength or pH from the embryo juice may counteract the effects of pulp phenolics bound to proteins in the throat or possibly compounds from the pulp may bind more preferentially to compounds from the embryo [25]. Overall, the seed tissues have more total phenolics, antioxidant effects and antifungal activity than the pulp tissues, indicating there may be other beneficial health effects of the seeds that may be different than the pulp [13].

6.2 Fruit pulp tissues

The ethnomedicinal uses of the pulp tissues are associated with the potential biological activities of several of the phytochemicals identified in the pulp tissues (Table 2). The use of the pulp for treatment of hypertension may be explained in part by caffeic acid, which effectively inhibited vascular smooth muscle cell proliferation in rats induced by angiotensin II, or had antihypertensive effects in a stroke-prone animal model [26]. However, coumaric acid derivatives identified in the pulp tissues are more likely to explain the use of the pulp for treatment of hypertension. *p*-Coumaric acid has antioxidant effects and anti-platelet activity in humans at doses that can be obtained with dietary intervention [27]. Furthermore, a coumaric acid sugar derivative was confirmed as one of the major peaks in the HPLC fingerprint profile of the pulp at 280 nm [11].

The presence of *p*-coumaroyl hexose (glucose or galactose) was also confirmed by mass spectrometry in the semi-purified pulp fraction that exhibited antimicrobial activity [3, 11, 13]. The use of the pulp for treatment of diarrhea may be due to astringent polyphenolics, or antimicrobial hydroxycinnamic acids (e.g., coumaric acid) that target the source of this condition [9, 28]. Coumaric acid and derivatives are effective inhibitors of several types of bacteria including *E. coli* [28]. *p*-Coumaric acid was reported to be absorbed by all digestive organs in rats and not metabolized significantly, suggesting this compound may exert biological activities, including antimicrobial and antioxidant effects, effectively in the gastrointestinal region of the body [29]. Thus, these fruits may potentially have similar effects as *L. chinesis* for treatment of ulcers and tumors in the gastrointestinal region; or as *D. longan*, and *N. lappaceum* for expelling parasites.

The use of the pulp for respiratory problems or asthma may also be in part due to the caffeic acid in the pulp, which is a selective inhibitor for the biosynthesis of leukotrienes, or compounds that sustain inflammatory reactions such as asthma [30]. The resveratrol derivatives identified in the pulp by mass spectroscopy may also explain the use of this part of the fruit for asthma and respiratory problems. This is because resveratrol acts as an inhibitor of NFκB, a transcripition factor involved in inflammation processes that lead to asthmatic symptoms [31].

The pulp tissues may be used for the treatment of constipation as a result of the ferulic acid derivatives identified in the pulp extracts. These derivatives may contribute to the laxative effects of the pulp tissues because ferulic acid and polar derivatives are reported to reduce colon transit time [32, 33]. Additionally, the ratio of glucose to fructose in these fruits is greater or equal to 1 and no sorbitol was detected in these fruits [11, 13]. This indicates that *M. bijugatus* fruit pulp may be less irritating to the digestive system, especially for sensitive individuals, and compared to fruits with more fructose than glucose (eg., apples) [3, 34].

In terms of toxicity, excessive pulp consumption may cause throat irritation due to the presence of astringent polyphenolics, or high amounts of coumaric acid, which is known to irritate the mucous membranes and upper respiratory tract at high concentrations [35]. However, no astringent catechins or derivatives were identified in the pulp. Hydroxycinnamic acids, unidentified phenolics or other compounds in the pulp may cause astringency [11, 25]. The toxic effects that result from consumption of the pulp tissues by adolescents, and possibly children, are likely to be caused by polyphenolics. High astringency in these fruits indicates the presence of compounds such as polyphenolics that not only bind to proteins but also chelate iron and other metals [3, 36, 37]. The presence of too many iron chelators in the diet can cause iron deficiency in adolescents, whose iron requirements are very high because of their rapid growth rate [36, 37].

Other toxicological activities are associated with the closely related species *Talisia squarrosa*, known to be used as a fish poison and likely to contain saponins [1, 10]. Saponins, have toxic effects in humans if present in high enough concentrations (e.g., hemolyze red blood cells), but are often associated with beneficial effects at possibly lower concentrations (e.g., lower plasma cholesterol concentrations) [38]. Consumption of potential saponins in the pulp of *M. bijugatus* fruits could reduce cholesterol and offer an additional explanation for using *M. bijugatus* pulp for the treatment of hypertension.

7. Conclusion

Ethnobotanical information combined with phytochemical data and chemotaxonomic details confirm the pulp and embryo of *M. bijugatus* fruits have both medicinal and dietary value for people. The use of *M. bijugatus* fruits as food, indicate the fruit pulp and the roasted embryo are relatively safe to consume in modest amounts. However, information obtained from ethnobotanical interviews suggests that the fruit pulp may have potential toxicological effects when consumed excessively or during periods of growth or high iron requirements.

The use of seed and pulp tissues of *M. bijugatus* fruits for gastrointestinal problems appear to be consistent with the uses of three other more commercial Sapindaceae fruit species. However, there are differences in specific uses among the species. Furthermore, the presence of coumaric acid derivatives or the absence of ellagic acid derivatives in the fruit tissues differentiates *M. bijugatus* fruits from the other species. Coumaric acid derivatives and catechin derivatives were the major known phenolics detected in the pulp and seed tissues, respectively [11]. These compounds, as well as other phenolics and specific sugar ratios in the fruits, may aid digestion, exert antimicrobial effects or have other beneficial effects on the gastrointestinal tract. Additionally, the treatment of hypertension with *M. bijugatus* pulp juice is a unique medicinal use in comparison to the seed tissues and the fruits of the other three Sapindaceae species.

Specific phenolics and sugars may explain some of the ethnomedicinal uses of *M. bijugatus* fruits, but other unidentified phenolics or other compounds, including saponins and nonpolar constituents, should also be investigated in these fruits for their biological effects. Currently, the only information available about the lipid-soluble compounds in these fruits come from a report that provides the carotenoid content of the fruit pulp (0.02–0.44 per 100 g of pulp) [2]. Moreover, different fruit varieties have different amounts of organic acids in the pulp (e.g., citric acid, succinic acid, malic acid and acetic acid), which may contribute to pH changes that affect the biological activities of phenolics or other phytochemcials [39].

This review demonstrates that compiling ethnobotanical and chemotaxonomic information, to interpret data from phytochemical investigations, is useful for predicting the biological activities of under-researched natural foods or medicines, such as *M. bijugatus* fruits.

Researching natural products that otherwise would be overlooked because of lack of financial endorsements, may be especially important to people in developing countries or areas where such natural resources may be prevalent but proper healthcare scarce. Furthermore, this review provides information that may be useful for predicting other medical uses and drug or food interactions of *M. bijugatus* fruits. Some of this information may also serve as springboard for research studies that more thoroughly examine the biological mechanisms of *M. bijugatus* fruit phyotchemicals for specific health conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

L.M.B. was funded by NIH training grant no. 5 T32 DK-007158 31. Information presented herein were part of a PhD thesis [3]. The author is grateful for the editorial advice from Dr. Ralph Obendorf; the Dominican Republic research trips organized by Dr. Eloy Rodriguez; my PhD advisors Dr. Betty Lewis and Dr. Dan Brown; fruit collection help and support from Wendy Meyer and Alicia and Richard Bystrom; and additional ethnobotanical information and fruits from Ceres Acuña, Pablo and Julian Lara (Lara's farm); Rolando Sano; Marcos Ramón and Mateo Restrepo.

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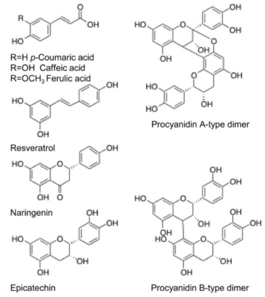

Fig. 1.

Select phenolics identified in *Melicoccus bijugatus* fruits. Many sugar derivatives of these compounds were also identified.

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Table 1

Ethnomedicinal information of *M. bijugatus* seed tissues in relation to phytochemistry and associated biological activities

Ethnomedicinal Information	Phytochemicals Identified [11].	Biological Activities of Phytochemicals
Treatment for diarrhea [2, 8]	Epicatechin, Procyanidins A-type procyanidins	Inhibit CFTR in Colon (prevents dehydration and nutrient loss) [20].
		Antimicrobial activity [21, 22].
General astringent [8]	Catechin dimer, catechin trimer	Tannins have astringent effects [23].
Treatment for parasites [6]	Naringenin	Anti-parasite activity against *Cryptosporidium parvum* and *Encephalitozoon intestinalis* [24].
Remedy for sore throat caused by excessive pulp consumption [3]	Chemicals that affect pH/ proteins or other compounds that bind to phenolics	pH change may affect binding affinity of irritants (e.g., phenolics) or these compounds may bind to other phytochemicals in seed juice [25].

Table 2

Ethnomedicinal information of *M. bijugatus* pulp tissues in relation to phytochemistry and associated biological activities

Ethnomedicinal information	Phytochemicals Identified [11]	Biological Activities of Phytochemicals
Hypertension [7]	Caffeic acid,	Inhibits vascular smooth muscle cell proliferation induced by angiotensin II in stroke-prone hypertensive rats [26].
	Coumaric acid	Anti-platelet activity *in vivo* and *in vitro* [27].
Asthma and respiratory problems [8]	Caffeic acid	A selective inhibitor for leukotriene biosynthesis [30].
	Resveratrol	Reported as a strong, broad-spectrum nonspecific inhibitor of the activation of NFκB in several cell lines [31].
Constipation/gastrointestinal discomfort [8]	Ferulic acid	Reduces colon transit time in rats [32, 33].
	Glucose/fructose ratio is ≥ 1	Easily digested and less irritating for digestive problems [34].
General Astringent [8]	Phenolics	Various types of phenolics have astringent effects [23, 25]
Diarrhea [9]	Phenolics	Astringency [23, 25].
	Hydroxycinnamic acids	Antimicrobial activity [28].
Causes throat irritation when consumed excessively [3]	High concentrations of *p*-coumaric acid	Irritates mucous membranes/ upper respiratory tract [35].
Avoided during puberty [3]	Phenolics	Can cause iron deficiency in people with rapid growth rate or high iron requirements [36, 37].