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Screening of Fifty *Cunoniaceae* Species from New Caledonia for Inhibitors of Xanthine Oxidase and Scavengers of Superoxide Anions

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Abstract

Two-hundred-and-four extracts (101 ethyl acetate extracts and 103 methanol extracts) from 50 species of *Cunoniaceae* from New Caledonia were screened for antioxidant properties due to free radical scavenging and/or xanthine oxidase (XOD) inhibitory activity. Of the crude extracts, 95.1% were active at a concentration of 50 µg/ml. Fifteen (27.8%) extracts showed more than 50% activity at 10 µg/ml and were studied for XOD inhibition. All were active against XOD at 50 µg/ml but only 6 (40%) showed up to 60% inhibition. Ethyl acetate extracts from the bark of *Weinmannia dichotoma* Brongniart & Gris, *Weinmannia monticola* Däniker and *Cunonia linearisepala* (Guillaumin) Bernardi and from the roots of *Codia incrassata* Pampanini, as well as methanol extract from the bark of *Pancheria brunhesii* Pampanini, exhibited the highest activities (between 70% and 86% XOD inhibition at 50 µg/ml). In view of these preliminary results, New Caledonian *Cunoniaceae* species appears to be promising material for the isolation of bioactive compounds.

Keywords: *Cunoniaceae*, ethyl acetate extract, free radical scavengers, methanol extract, New Caledonia, xanthine oxidase.

Introduction

In general, the biodiversity of New Caledonia is rich and unique. The flora, in particular, shows up to 80% endemicity (Jaffre et al., 1995), due to the Island's long geographical isolation after physical separation from Australia about 65 million years ago.

The flowering plant family Cunoniaceae, in the order Rosales (Cronquist, 1982), comprises 26 genera including more than 250 species (Heywood, 1985). It occurs largely in the southern hemisphere and is an example of this rich endemicity, since in New Caledonia, it contains 6 genera, *Acsmithia*, *Codia*, *Cunonia*, *Geissois*, *Pancheria* and *Weinmannia*, represented by more than 80 species, all of which are endemic (Guillaumin, 1948). Moreover, two of these genera, *Codia* and *Pancheria*, are endemic with 36 species all together.

Some members of the Cunoniaceae are reputed to have medicinal properties and are used to cure various diseases (Cambie & Ash, 1931; Rageau, 1957; Luis Diego Gomez, 1995). Because of this and the results of Bosisio et al. (2000), who showed that *Cunonia montana* Schlechter has anti-elastase and anti-xanthine oxidase activities, our laboratory decided to investigate several biological activities in this family, such as antibiotic effects, cytotoxicity and inhibition of different enzymes. Preliminary results show that some species present properties in all of these domains (Fogliani et al., 2000).

Xanthine oxidase (XOD) converts hypoxanthine to xanthine and finally to uric acid, the accumulation of which causes hyperuricacidemia associated with gout (Noro et al., 1983a; Hayashi et al., 1989). It is also responsible for oxidative damage to living tissues under conditions such as allergies, inflammation, diabetes, emphysema, heart ischemia-reperfusion, aging, atherosclerosis, etc. (Crastes de Poulet et al., 1994). Thus, free radical scavengers and/or specific inhibitors of XOD are expected to be therapeutically

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useful for the treatment of these pathologies (Goodman & Gilmans, 1990). Plant compounds such as xanthones, flavonoids, coumarins and proanthocyanidins have been reported to be potent inhibitors of xanthine oxidase (Sumahara et al., 1977; Noro et al., 1983b) and to possess anti-oxidant properties.

For these reasons, 50 species of Cunoniaceae from New Caledonia were assayed on XOD, using hypoxanthine and then xanthine as substrates. The objective was to select species with high activity and then to submit the active extracts for detailed phytochemical investigations in order to isolate the bioactive constituents.

Materials and methods

Plant material

Material was collected by Bruno Fogliani from localities in New Caledonia at different seasons but always from plants in flower or fruit. All accessible parts were sampled, including leaves, bark, flowers, fruits and roots, and herbarium voucher specimens were made. Identifications were made by comparison with named collections in the herbarium at the Institut de la Recheche pour le Developpement (I.R.D.), Nouméa, and some were verified by Helen Fortune Hopkins (Lancaster University) and Jason Bradford (Missouri Botanical Garden) who are currently revising some genera of New Caledonian Cunoniaceae. Voucher specimens were deposited in our laboratory (L.B.P.V.A.) in the University of New Caledonia. Samples are referred to as BF 1–90.

Preparation of the crude extracts

Two samples of 10 g each of the air-dried powdered plant material were extracted separately by maceration for 24 h with ethyl acetate (100 ml) and methanol (100 ml). After filtration, the extracts were concentrated in *vacuo* at 45 °C and weighed for the determination of the w/w yield. The residue was dissolved in methanol to a concentration of 1 mg/ml for the tests.

Test solutions

Crude extracts in methanol were diluted in buffer to obtain the desired final concentrations of 50, 10 and 1 µg/ml in the reaction mixture as described by Gonzales et al. (1995).

Reagents

XOD (EC 1.1.3.22) from buttermilk (Grade III, 1.1 units/mg protein), hypoxanthine, xanthine, nitroblue tetrazolium, quercetin and all other reagents and chemicals were purchased from the Sigma Chemical Company. In the assay with hypoxanthine substrate, all products were dissolved and diluted with 0.05 M Tris-HCl buffer, pH 7.5, while in the case of xanthine substrate, this was done in 0.1 M K^+ phosphate buffer, pH 7.8.

Activity assay with hypoxanthine as substrate

At first, all the extracts were tested with hypoxanthine as substrate to find XOD inhibitory activity and/or antioxidant properties due to free radical scavenging. This phenomenon was measured spectrophotometrically following the conversion of nitroblue tetrazolium (NBT) to formazan, at 560 nm for 3 min, as reported by Bors et al. (1989).

The assay mixture consisted of 100 µl test solution, 500 µl of hypoxanthine (5 µM), and 100 µl of NBT (1 mM). After preincubation of the mixture at 25 °C for 15 min, the reaction was initiated by adding 100 µl of enzyme solution (1.67 U/ml) and stopped after 3 min of incubation by adding 100 µl of HCl (1 N). Variation of absorbance was measured against a blank prepared in the same way except that the enzyme solution was added to the assay mixture after adding HCl. Percent activity was calculated according to the following formula: (1-B/A) × 100, where A is the absorbance without the test material and B the absorbance with the test material. All crude extracts with an activity up to 60% at 50 µg/ml were then tested at concentrations of 10 and 1 µg/ml. Extracts showing an activity up to 50% at 10 µg/ml were then assayed with xanthine as the substrate, in order to determine whether the activity was due to xanthine oxidase inhibition.

XOD activity assay

The enzyme activity was measured spectophotometrically at 295 nm following the conversion of xanthine to uric acid for 3 min as reported by Robak et al. (1988), with the following modifications. The assay mixture contained 0.1 M K+-phosphate buffer, pH 7.8, 10 µM EDTA, 0.1 mM xanthine and 0.04 units/ml XOD, with a final volume of 1 ml. This mixture was preincubated for 15 min at 25 °C with the test material before adding the substrate. The reaction was stopped by adding 100 µl of 1 N HCl and the variation of absorbance was measured against a blank prepared in the same way except that the enzyme solution was added to the assay mixture after adding HCl. XOD inhibitory activity was expressed as the percentage of inhibition calculated as (1-B/A) × 100, as described above. The selected extracts were tested at 50 µg/ml and extracts with activity up to 60% were then tested at 10 and 1 µg/ml. Quercetin (3.4 µg/ml) was used as reference inhibitor.

Results and discussion

Two hundred and four extracts from 50 species of New Caledonian Cunoniaceae were assayed for anti-oxidant properties due to free radical scavenging and/or XOD inhibitory activity at a concentration of 50 µg/ml. The results are shown in Table 1. Of all the extracts assayed, 194 (95.1%) demonstrated an activity at 50 µg/ml. Among these, 54 (26.5%) extracts showed an activity above 60% at that concentration.

Table 1. Extraction yield (% starting material, w/w) and % of activity.

Genera/Species voucher specimen	Plant part	Extract	Yield	Activity (%)[a]		
				50 µg/ml	10 µg/ml	1 µg/ml
Acsmithia						
Acsmithia elliptica	Leaves	AcOEt	2.3	50.1		
(Vieillard ex Pampanini) Hoogland		MeOH	14.4	54.5		
(BF 58)	Bark	AcOEt	2.3	28.6		
		MeOH	17.1	64.4	26	1.4
Acsmithia meridionalis	Leaves	AcOEt	6.6	10.2		
Hoogland (BF 70)		MeOH	7.3	31.4		
	Bark	AcOEt	3.3	18.9		
		MeOH	5.7	41.7		
Acsmithia pedunculata	Leaves	AcOEt	1.9	19.1		
(Schlechter) Hoogland (BF 69)		MeOH	5.2	32.1		
	Bark	AcOEt	1.5	10.3		
		MeOH	4	40.3		
Acsmithia pubescens	Leaves	AcOEt	2.8	30.7		
Pampanini (BF 34)		MeOH	13	34.1		
	Bark	AcOEt	3.8	23.9		
		MeOH	16.7	54.6		
Codia						
Codia albifrons	Leaves	AcOEt	2.5	12.6		
Vieillard ex Guillaumin (BF 83)		MeOH	8.5	37.5		
	Bark	AcOEt	0.5	47.9		
		MeOH	4.7	37.8		
Codia arborea	Leaves	AcOEt	0.9	31		
Brongniart ex Guillaumin (BF 14)		MeOH	7.2	64.9	18.1	8.4
	Bark	AcOEt	0.7	81.1	78.2	45.5
		MeOH	4.2	73.7	18.7	12.5
Codia discolor	Leaves	AcOEt	1.9	62.4	16.8	0
(Brongniart & Gris) Guillaumin (BF 55)		MeOH	11.6	72.1	39.5	9.7
	Bark	AcOEt	1.7	47.6		
		MeOH	16.3	77.5	35.6	8.8
	Flowers	AcOEt	0.5	32.1		
		MeOH	3.4	40		
Codia ferruginea	Leaves	AcOEt	2.3	1.2		
Brongniart & Gris (BF 88)		MeOH	9.2	74.6	18	3.8
	Bark	AcOEt	0.7	68.8	6.7	0
		MeOH	8.2	46.3		
Codia incrassata	Leaves	AcOEt	1.3	9.4		
Pampanini (BF 36)		MeOH	15.4	40.3		
	Bark	AcOEt	1.1	54.1		
		MeOH	11.6	70.5	42.6	14.2
	Roots	AcOEt	1.2	62.1	50.2	0
		MeOH	9.3	77.8	26.9	10.4
Codia montana	Leaves	AcOEt	1.7	56.9		
Forster (BF 37)		MeOH	9	77.9	47.2	9.5
	Bark	AcOEt	1.7	55.1		
		MeOH	4	76.1	20.2	0
	Roots	AcOEt	1.1	76.3	34.7	0
		MeOH	13.5	67.9	12.1	0
Codia nitida	Leaves	AcOEt	1.8	49		
Schlechter (BF 62)		MeOH	16	72.8	52.2	28.5
	Bark	AcOEt	1.1	59.7		
		MeOH	10.2	73.6	50.4	28.5
Codia sp nov.	Leaves	AcOEt	1.1	13.5		
(BF 84)		MeOH	12.9	41.3		
	Bark	AcOEt	1.5	12.5		
		MeOH	5.8	80.9	23.9	0

Table 1. Continuted

Genera/Species voucher specimen	Plant part	Extract	Yield	Activity (%)[a] 50 µg/ml	10 µg/ml	1 µg/ml
Cunonia						
Cunonia alticola	Leaves	AcOEt	2.1	51.5		
Guillaumin (BF 59)		MeOH	28.4	52.3		
	Bark	AcOEt	0.9	50.8		
		MeOH	9.5	53.1		
Cunonia aoupiniensis	Leaves	AcOEt	2.9	21.6		
Hoogland (Lit 048*)		MeOH	2.4	48.5		
Cunonia atrorubens	Leaves	AcOEt	3.9	53.6		
Schlechter (BF 52)		MeOH	12.5	44.6		
	Bark	AcOEt	2.2	18.1		
		MeOH	13	52.9		
Cunonia austrocaledonica	Leaves	AcOEt	2.3	41.8		
Brongniart & Gris ex Guillaumin		MeOH	9	26.4		
(BF 79)	Bark	AcOEt	0.9	72.6	50.3	44.7
		MeOH	0.6	48.7		
Cunonia bullata	Leaves	AcOEt	4	14.2		
Brongniart & Gris (BF 67)		MeOH	4.3	22.1		
	Bark	AcOEt	1.7	12.9		
		MeOH	3.2	26.8		
Cunonia balansae	Leaves	AcOEt	1.7	37.6		
Brongniart & Gris (BF 54)		MeOH	9.7	61.1	0	0
	Bark	AcOEt	1.3	33		
		MeOH	9.8	75.1	23.5	2.8
	Fruit	AcOEt	1.4	43.8		
		MeOH	5.3	85.2	28.4	3.1
Cunonia deplanchei	Leaves	AcOEt	3.9	37.8		
Brongniart & Gris (BF 17)		MeOH	5.6	11.4		
	Bark	AcOEt	0.7	9.3		
		MeOH	2.8	77.4	20.9	0
Cunonia lenormandii	Leaves	AcOEt	1.4	8.7		
Vieillard ex Brongniart & Gris (BF 66)		MeOH	7.6	0.1		
	Bark	AcOEt	4.1	10.8		
		MeOH	2.2	28		
Cunonia linearisepala	Leaves	AcOEt	2.6	20.1		
(Guillaumin) Bernardi (BF 81)		MeOH	8.8	51.5		
	Bark	AcOEt	1.9	88.7	50.9	9.8
		MeOH	3.2	53.6		
Cunonia macrophylla	Leaves	AcOEt	2.4	37.6		
Brongniart & Gris (BF 53)		MeOH	18	76.9	27.8	10.3
	Bark	AcOEt	0.7	30.4		
		MeOH	13	76.1	20.6	0
	Flowers	AcOEt	2.3	61.8	9.2	2.2
		MeOH	17.5	88.7	27.1	25.6
Cunonia montana	Leaves	AcOEt	0.7	48.3		
Schlechter (BF 57)		MeOH	10.2	52.8		
	Bark	AcOEt	1.1	54.5		
		MeOH	16.4	57.1		
Cunonia pulchella	Leaves	AcOEt	1.1	47.4		
Brongniart & Gris (BF 35)		MeOH	8	16.8		
	Bark	AcOEt	0.6	52.3		
		MeOH	11	56.7		
Cunonia pterophylla	Leaves	AcOEt	0.8	25.9		
Schlechter (BF 13)		MeOH	3.9	49.1		
	Bark	AcOEt	0.6	21.1		
		MeOH	4.7	70.8	13	12.5

Table 1. Extraction yield (% starting material, w/w) and % of activity.

Genera/Species voucher specimen	Plant part	Extract	Yield	Activity (%)[a] 50 µg/ml	10 µg/ml	1 µg/ml
Cunonia purpurea	Leaves	AcOEt	1.3	7.9		
Brongniart & Gris (BF 48)		MeOH	10	13.9		
	Bark	AcOEt	1.4	78.3	54.6	35.9
		MeOH	10	51		
Cunonia rotundifolia	Leaves	AcOEt	0.8	0		
Däniker (BF 68)		MeOH	7.1	78.9	50.2	9.7
Cunonia varijuga	Leaves	AcOEt	0.7	52.2		
Hoogland (BF 28)		MeOH	7.5	46.9		
	Bark	AcOEt	0.3	22.9		
		MeOH	9.4	50.4		
Cunonia vieillardii	Leaves	AcOEt	4.3	0		
Brongniart & Gris (BF 89)		MeOH	10.6	87.6	27.9	5.5
	Bark	AcOEt	0.5	29.2		
		MeOH	3	51.6		
Geissois						
Geissois hippocastaneifolia	Leaves	AcOEt	1.5	18.6		
Guillaumin (BF 23)		MeOH	18	31.3		
	Bark	AcOEt	0.4	20.7		
		MeOH	14.5	51.6		
Geissois hirsuta	Leaves	AcOEt	1.4	0		
Brongniart & Gris (BF 29)		MeOH	3	39.3		
	Bark	AcOEt	3.1	75.6	28.9	1.6
		MeOH	3.4	56.6		
Geissois polyphylla	Leaves	AcOEt	1.4	1.1		
Lecard ex Guillaumin (BF 38)		MeOH	8.5	24.1		
	Bark	AcOEt	0.4	55.3		
		MeOH	10.2	54		
Geissois pruinosa	Leaves	AcOEt	2.5	30.6		
Brongniart & Gris (BF 15)		MeOH	4.8	36		
	Bark	AcOEt	0.4	34		
		MeOH	5.9	49		
Geissois magnifica	Leaves	AcOEt	1.1	30.1		
Baker (BF 24)		MeOH	8.5	45.5		
	Bark	AcOEt	0.7	26.3		
		MeOH	12	63.7	20	6.3
Weinmannia						
Weinmannia dichotoma	Leaves	AcOEt	4.4	36.8		
Brongniart & Gris (BF 40)		MeOH	12.7	59.9		
	Bark	AcOEt	5.9	95.9	54.1	32.**8**
		MeOH	14.4	53.8		
Weinmannia monticola	Leaves	AcOEt	5.2	43.2		
Däniker (BF 39)		MeOH	13.7	54		
	Bark	AcOEt	6.6	91.9	67.9	16.9
		MeOH	13.6	58.7		
Pancheria						
Pancheria alaternoides	Leaves	AcOEt	1.7	10.1		
Brongniart & Gris (BF 12)		MeOH	12.9	60.6	9.6	0
	Bark	AcOEt	0.8	8.1		
		MeOH	11.3	71.2	15.2	0
Pancheria brunhesii	Leaves	MeOH	4.4	50.7		
Pampanini (BF 16)	Bark	MeOH	3.8	87.2	50.8	10.5
Pancheria communis	Leaves	AcOEt	2.7	14.7		
Baker (BF 82)		MeOH	8.1	41.9		
	Bark	AcOEt	0.6	24.2		
		MeOH	6.5	33.9		

Table 1. Continuted

Genera/Species voucher specimen	Plant part	Extract	Yield	Activity (%)[a] 50 µg/ml	10 µg/ml	1 µg/ml
Pancheria confusa	Leaves	AcOEt	1.3	10.5		
Guillaumin (BF 21)		MeOH	13.6	39.7		
	Bark	AcOEt	1.3	12.4		
		MeOH	12.1	68.7	31	9
Pancheria elegans	Leaves	AcOEt	3.9	4.8		
Brongniart & Gris (BF 78)		MeOH	10.3	27.4		
	Bark	AcOEt	1.1	0		
		MeOH	3.8	29.6		
Pancheria elliptica	Leaves	AcOEt	3.9	37.8		
Pampanini (BF 20)		MeOH	11.9	65	27.2	0.6
	Bark	AcOEt	1.3	29.5		
		MeOH	10.2	92.1	33.9	5.5
Pancheria engleriana	Leaves	AcOEt	1.8	43.2		
Schlechter (BF 56)		MeOH	9.7	47.4		
	Bark	AcOEt	0.7	63.1	31.7	2.3
		MeOH	13.2	68.1	13.7	0
Pancheria ferruginea	Leaves	AcOEt	2.9	36.6		
Brongniart & Gris (BF 61)		MeOH	15.3	75.7	50.7	15.7
	Bark	AcOEt	1.6	68.5	34.7	0
		MeOH	11.3	79	56.4	39.9
Pancheria hirsuta	Leaves	AcOEt	3.3	16.1		
Vieillard ex Pampanini (BF 22)		MeOH	12.6	43.4		
	Bark	AcOEt	0.5	55.6		
		MeOH	2.2	21.9		
Pancheria obovata	Leaves	AcOEt	4	14.4		
Brongniart & Gris (BF 51)		MeOH	10	43.1		
	Bark	AcOEt	0.9	80.2	50.1	26.6
		MeOH	10	33.6		
Pancheria phylliraeoides	Leaves	AcOEt	6.3	0		
Brongniart & Gris ex Guillaumin		MeOH	11.2	52.3		
(BF 85)	Bark	AcOEt	0.5	62.4	10.7	0
		MeOH	12.7	49.4		
Pancheria reticulata	Leaves	AcOEt	4.3	20.7		
Guillaumin (BF 60)		MeOH	19.7	49.9		
	Bark	AcOEt	0.6	89.2	22.8	15.2
		MeOH	13.4	71.4	50.49	0
Pancheria sebertii	Leaves	AcOEt	5.8	0		
Guillaumin (BF 86)		MeOH	9.2	59.5		
	Bark	AcOEt	1.5	72.9	18.8	5.1
		MeOH	5.5	51.3		
Pancheria vieillardii	Leaves	AcOEt	5.2	1.1		
Brongniart & Gris (BF 87)		MeOH	7.9	55.9		
	Bark	AcOEt	1.5	69	11.1	4.7
		MeOH	8	38		

[a] Mean 9 determinations. In control samples, Δabs was 0.303 ± 0.05/min for activity with hypoxanthine as substrate (mean ± s.e.; n = 20).
* plant powder from Mr Marc Litaudon, C.N.R.S center of Noumea.

All of these were then tested at 10 and 1 µg/ml. At 10 µg/ml, 53 (98.1%) of the extracts were active; 15 (27.8%) showed activity over 50%. At 1 µg/ml, 36 (66.6%) were still active.

It is clear from Table 1 that the genera *Acsmithia* and *Geissois* are the least interesting for further studies. In contrast, the endemic genera *Codia* and *Pancheria* appear to be good potential sources of bioactive compounds, as an activity of over 60% at 50 µg/ml was showed by, respectively, 87.5 and 75% of the species tested. These values represent 18 (47.4%) of the extracts from *Codia* species and 15 (32.6%)

Table 2. Extraction yield (% starting material, w/w) and XOD inhibition.[a]

Genera/Species voucher specimen	Plant Part	Extract	Yield	Inhibition (%)[b] 50 µg/ml	10 µg/ml	1 µg/ml	IC_{50}
Codia							
Codia arborea Brongniart ex Guillaumin (BF 14)	Bark	AcOEt	0.7	44.1			
Codia incrassata Pampanini (BF 36)	Roots	AcOEt	1.2	69.9	17.1	0.8	41.8
Codia nitida	Leaves	MeOH	16	50.6			
Schlechter (BF 62)	Bark	MeOH	10.2	49.4			
Cunonia							
Cunonia austrocaledonica Brongniart & Gris ex Guillaumin (BF 79)	Bark	AcOEt	0.9	34.6			
Cunonia linearisepala (Guillaumin) Bernardi (BF 81)	Bark	AcOEt	1.9	81.7	10.2	1.8	33.1
Cunonia purpurea Brongniart & Gris (BF 48)	Bark	AcOEt	1.4	38.2			
Cunonia rotundifolia Däniker (BF 68)	Leaves	MeOH	7.1	62.1	0	0	nd
Weinmannia							
Weinmannia dichotoma Brongniart & Gris (BF 40)	Bark	AcOEt	5.9	82.2	18.9	2.8	22.4
Weinmannia monticola Däniker (BF 39)	Bark	AcOEt	6.6	86.1	19.2	3.4	30.2
Pancheria							
Pancheria brunhesii Pampanini (BF 16)	Bark	MeOH	3.8	72.1	10.6	1.5	28.7
Pancheria ferruginea	Leaves	MeOH	15.3	30.3			
Brongniart & Gris (BF 61)	Bark	MeOH	11.3	31.7			
Pancheria obovata Brongniart & Gris (BF 51)	Bark	AcOEt	0.9	31.5			
Pancheria reticulata Guillaumin (BF 60)	Bark	MeOH	13.4	54.1			

[a] Under the described experimental conditions, quercetin 10 µM (3.4 µg/ml) gave an inhibition of 58.8 ± 2.2% (mean ± s.e.; n = 12 assays).
[b] Mean of nine determinations. In control samples, Δabs was 0.251 ± 0.05/min for XOD activity (mean ± s.e.; n = 20 assays).

of those from *Pancheria* species. The genus with the highest activities, *Weinmannia*, was represented here by two species among the five existing in New Caledonia, although Hopkins (1998) considered there are only four species and placed *Weinmannia monticola* Däniker into synonomy with *Weinmannia dichotoma* Brongniart & Gris. Both species of *Weinmannia* tested here gave similar results, which may perhaps support this conclusion.

At this stage of our investigations, we arbitrarily decided that we should only conserve the 15 extracts with activity up to 50% at 10 µg/ml for further studies. All of them were tested for XOD inhibitory activity at 50 µg/ml; results are shown in Table 2. All demonstrated XOD inhibitory activity, but only 6 (40%) showed enzyme inhibition of over 60% at this concentration. The nine less active extracts probably possessed both free radical scavengers and inhibitors of xanthine oxidase.

The six with the highest XOD inhibitory activities were then tested at 10 and 1 µg/ml. Five of them were active at these concentrations; their IC_{50} values were calculated and are given in Table 2. It is interesting to note that except for the extract obtained from the roots of *Codia incrassata* Pampanini, all are extracts of bark, and three are ethyl acetate extracts.

It thus appears that five species, *Codia incrassata* Pampanini, *Cunonia linearisepala* (Guillaumin) Bernardi, *Weinmannia dichotoma* Brongniart & Gris, *Weinmannia monticola* Däniker and *Pancheria brunhesii* Pampanini, are encouraging starting materials for the further isolation of compounds with anti-XOD activities. In our experimental conditions, XOD inhibition by 10 µM (3.4 µg/ml) quercetin was 58.8 ± 2.2% (mean ± s.e.; n = 12 assays), while the IC_{50} for quercetin has been reported as 10 µM (Robak et al.,1988). In comparison, our extracts from the five species cited above,

showed XOD inhibitory activities between 70 and 86% at a concentration of 50 µg/ml.

In conclusion, based on these results, Cunoniaceae from New Caledonia seem to be a very promising source for the isolation of active molecules, through a bioassay guided fractionation, that could be used from a therapeutic perspective against gout and in the treatment of free radical tissues injuries.

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