

Chapter

Phytochemical Study and Biological Activities of Endemic Species of *Vaccinium* from French Polynesia

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Abstract

French Polynesia is a natural laboratory with over 53% of endemism in its vascular terrestrial flora. The flora remains little studied from a phytochemical point of view. In order to overcome this lack of knowledge, we were interested in an endemic taxon from the specie *Vaccinium cereum*, also named as “opu opu.” Four varieties of *V. cereum* are present in French Polynesia: var. *adenandrum* (Decne) F.Br, var. *cereum* (L.f.) G. Forst, var. *pubiflorum* Skottsb and var. *raiateense* M.L. Grant. All four showed comparable antioxidant and antiradical activities and inhibitory activity against α -glucosidase. Leaves of *V. cereum* var. *cereum* carry out a bio-guided phytochemical study. Among the isolated compounds, NMR has characterized ursolic acid, oleanolic acid, chlorogenic acid, astragalins, and isoquercitrin, as the major active compounds. The results revealed that this taxon represents a real health benefit and might have promising proprieties to regulate blood sugar.

Keywords: *Vaccinium cereum*, phytochemical studies, biological activities, endemism, French Polynesia

1. Introduction

French Polynesia is a French overseas collectivity composed of 118 islands spread over an area as large as continental Europe. Its geographical situation, its isolation, and its tropical climate give French Polynesia a rich and original terrestrial flora.

The native vascular flora of French Polynesia has about 870 species, of which 460 are endemic, or 54% of this flora. Some species are endemic to an archipelago, an island, or even a valley or a mountain. Conserving this biodiversity, as well as finding the right balance between protecting and benefiting from this resource has been a widely accepted concept since the adoption of the Convention on Biological Diversity (CBD) in Rio in 1992.

Diabetes represents one of the largest health problems in the world, affecting more and more people each year, with an estimated total burden of death due to high blood sugar in 2020 of 4 million [1, 2].

In 2017, according to figures from the IDF (International Diabetes Federation), 425 million people had diabetes. IDF estimates that the number of people with diabetes

will increase by 48% worldwide by 2045. These rates of increase may reach 82% in Southeast Asia and 156% in Africa [3].

In French Polynesia, 10% of the population has diabetes. This disease remains the second most common chronic noncommunicable disease after hypertension. The number of patients diagnosed in 10 years (from 2001 to 2012) has doubled and continues to increase. This disease raises real social, political, and economic issues for the future of French Polynesia: it cost nearly 30 million euros in health care expenses, added to various patient complications.

Diabetes is a health priority in French Polynesia [4]. In addition to the diabetes campaigns conducted by the French Polynesian Health Department for more than 15 years, the search for new treatments remains important, both locally and globally.

Numerous plant-based preparations are described in traditional medicine for the prevention of diabetes but have not been the subject of real treatments due to a lack of laboratory studies. In the last decades, several works on the mode of action and the targets of these preparations could revive the interest in the use of plants in the treatment and prophylaxis of type two diabetes, T2DM.

Table 1 describes some plants or plant preparations used to treat T2DM. This list is not exhaustive; it cites plants used in traditional medicine worldwide and studied for their antidiabetic effect.

Many plants are used for their hypoglycemic effect. In general, the preparations combine several plants and can be administered in different forms: dry extracts (capsules, herbal teas), essential oils, or mother tinctures. In addition, in the context of antidiabetic treatment, the use of antioxidants in supplementation helps prevent the appearance of complications related to oxidative stress [5–11].

In this context, the first research program allowed to perform a screening on different biological targets from several extracts of terrestrial and marine organisms targeting Alzheimer's disease, melanoma, and diabetes. Thus, pharmacological screening on enzymatic targets (acetylcholinesterase, α -glucosidase, and tyrosinase) subject 117 marine extracts and 228 extracts from Polynesian terrestrial flora (from 122 species).

This work has allowed highlighted the strong inhibitory activity of the ethanolic extract of *Vaccinium cereum* var. *cereum* leaves toward α -glucosidase, an enzyme involved in the regulation of blood sugar and the control of T2DM.

2. *Vaccinium* sp.

The genus *Vaccinium* (bilberries, blueberries, and cranberries) is a member of the Ericaceae family, which includes more than 340 species in 87 genera.

In 1933, there were 160 species belonging to the genus *Vaccinium* distributed between the northern hemisphere and the mountains of tropical regions.

In 2014, Northern Hemisphere described 450 species. Many of them are cultivated for their berries as they are often edible.

The antidiabetic properties of plants of the genus *Vaccinium* were first cited in 1892. The infusion of bilberry leaves would decrease glycosuria [12].

Research on the use of the aqueous extract of *Vaccinium* as an antidiabetic agent mobilized the scientific world until 1936, with suspicion of the presence of toxic hydroquinones. In 1996, *Vaccinium myrtillus* demonstrated the absence of hydroquinone, which re-launched research on the antidiabetic properties of *Vaccinium* extracts' [12].

Plant	Preparation	Plant part	Use and therapeutic target
<i>Allium cepa</i>	Raw, infusion, mother tincture	Bulbs	Hypoglycemic, antioxidant
<i>Allium sativum</i>	Raw, freeze-dried powder, alcoholic tincture	Bulbs	Hypoglycemic
<i>Anacardium</i> sp.	Ethanollic extract	Barks	Hypoglycemic <i>in vivo</i>
<i>Artocarpus altilis</i>	Methanolic extract	Bark and fruits	Inhibition of α -glucosidase and α -amylase [5]
<i>Artocarpus heterophyllus</i>	Methanolic extract	Sheets	Inhibition of α -glucosidase and α -amylase [5]
<i>Cinnamomum zeylanicum</i>	Methanolic extract	Sheets	Inhibition of α -glucosidase and α -amylase [5]
<i>Eucalyptus globulus</i>	Powder	Sheets	Hypoglycemic
<i>Ficus benghalensis</i>	Decoction	Barks	Hypoglycemic <i>in vivo</i> [6]
<i>Moringa oleifera</i>	Ethanollic extract	Sheets	Hypoglycemic <i>in vivo</i>
<i>Piper betle</i>	Methanolic extract	Sheets	Inhibition of α -glucosidase and α -amylase [5]
<i>Phyllanthus amarus</i>	Ethanollic extract and decoction	Sheets	Reduction of blood glucose [7]
<i>Prosopis africana</i>	Ethanollic extract	Barks	Hypoglycemic <i>in vivo</i>
<i>Punica granatum</i>	Methanolic extract	Flowers	Inhibition of α -glucosidase [8]
<i>Ramulus mori</i>	Decoction	Branches	Inhibition of α -glucosidase [9]
<i>Rosa sinensis</i>	Infusion	Flowers	Hypoglycemic
<i>Sclerocarya birrea</i>	Ethanollic extract	Roots	Hypoglycemic <i>in vivo</i>
<i>Syzygium cumini</i>	Aqueous extract	Branches	Hypoglycemic, α -amylase inhibitor [10]
<i>Vaccinium angustifolium</i>	Alcoholic extract	Sheets	Insulin-like and glitazone-like. Promotes the proliferation of pancreatic cells
<i>Vaccinium myrtillus</i>	Alcoholic extract	Sheets	Hypoglycemic

Table 1.
Use of herbs in the treatment of type 2 diabetes.

Table 2 summarizes some recent research on the antidiabetic properties of organic extracts and molecular families isolated from different *Vaccinium* species.

2.1 *Vaccinium cereum* (L.f.) G.Forst

In French Polynesia, two endemic species, whose berries are edible, are present [22]: *Vaccinium cereum* (L.f.) G.Forst and *Vaccinium rapae* Skottsbo.

V. rapae being an endangered species listed on the red list of threatened species in France, the study was conducted only on the species *V. cereum* (**Figure 1**).

Several vernacular names are used to refer to *Vaccinium cereum* as “opu opu” in Tahiti, “heua” or “heuki” in Nuku Hiva and “puatoatoa” in Fatu Hiva [22]. It is endemic to Polynesia. Present in the Society archipelago, the Marquesas

Species	Plant part	Extract/family of molecules studied	Mode of action
<i>Vaccinium angustifolium</i>	Roots	Ethanolic extract	Transport of glucose to cells [13]
	Barks	Ethanolic extract	Transport of glucose to cells, stimulates insulin secretion [13]
	Sheets	Ethanolic extract	Transport of glucose to cells, stimulates insulin secretion [13]
	Fruits	Anthocyanins	Proliferation of β -pancreatic cells [13] Stimulates insulin secretion [14]
<i>Vaccinium arctostaphylos</i>	Fruits	Hydroxycinnamic acid, phenolic compounds anthocyanins	Inhibits α -glucosidase and stimulates insulin secretion [15]
	Sheets	Flavonoids anthocyanins	Inhibition of α -amylase Stimulates insulin secretion [16]
<i>Vaccinium ashei</i>	Sheets	Glucosidic flavonol, substituted phenylpropanoid-3-ols, anthocyanins, proanthocyanidins	Inhibition of α -glucosidase [17, 18]
	Fruits	Aqueous acetone extract (50%)	Inhibition of α -glucosidase [19]
<i>Vaccinium bracteatum</i>	Sheets	Polysaccharides	Stimulates insulin secretion [19]
<i>Vaccinium corymbosum</i> var. <i>jersey</i>	Fruits	Aqueous acetone extract (50%)	Inhibition of α -glucosidase [19]
	Flowers	Hydroxycinnamic acid, glucoside flavonol, phenylpropanoid-substituted catechin	Inhibition of α -glucosidase [19]
<i>Vaccinium myrtillus</i>	Sheets	Aqueous ethanolic extract (40%)	Transport of glucose to cells [20]
<i>Vaccinium vitis-idaea</i>	Fruits	Glucosidic flavonols	Transport of glucose to cells [21]

Table 2.

Organic extracts and hypoglycemic molecules isolated from the genus Vaccinium.

archipelago, and the Cook Islands, *V. cereum* grows at altitudes above 500 m, notably up to the summit of Mount Aorai (2064 m), one of the highest peaks of the island of Tahiti. Observed also at lower altitudes, the shrubs are smaller.

It is a shrub of 2 to 2.5 m in height. The wood is very hard and quite dense. The leaves on the old branches are large, leathery, and elliptical (5×3.5 cm), while they are thinner, smaller, and generally obovate (average 2.3×1.6 cm) on the flowering stems. They are persistent for 3–4 years, shiny above, paler below.

The flowers are permanent throughout the year. They are axillary, solitary, on a stalk 5 to 8 mm, and about 1 cm long. The corolla is white, or with a pink to red tip [22] and a cinnamon-vanilla perfume.

The fruits, edible but very little consumed, are red, dark purple to black, of approximately 1.5 cm in diameter. The pubescence of the flowers is very variable. On this last criterion, Skottsberg determined a certain number of varieties or taxa.

In French Polynesia, four taxa of *Vaccinium cereum* are recognized (**Figure 2**):

- *Vaccinium cereum* var. *adenandrum* (Decne.) F.Br., endemic to the Marquesas Islands;

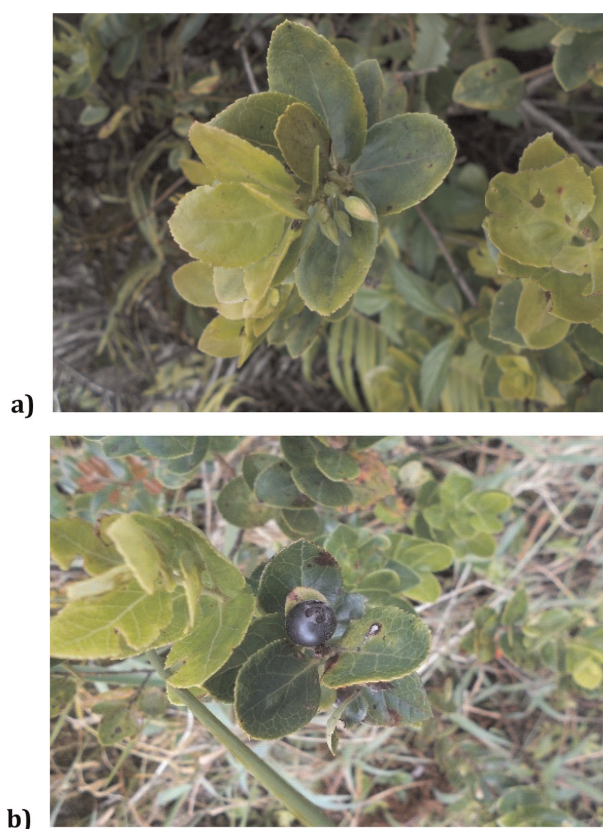


Figure 1.
 a) Flower buds and b) fruit of *Vaccinium cereum* var. *cereum* (Photo credit S. Benayad).

- *Vaccinium cereum* var. *cereum*, (L.f.) G.Forst., endemic to the Society Archipelago;
- *Vaccinium cereum* var. *pubiflorum* Skottsbo, endemic to the Society Archipelago;
- *Vaccinium cereum* var. *raiateense* M.L.Grant, endemic to the island of Raiatea (Society Archipelago).

In order to enhance *Vaccinium cereum*: A comparative study of the biological activity of the different taxa found in French Polynesia (*V.c.* var. *cereum*, *V.c.* var. *adenandrum*, *V.c.* var. *pubiflorum*, *V.c.* var. *raiateense*) has been carried out *V.c.* var. *raiateense* being an endangered taxon listed on the red list of threatened species in France only a few leaves were collected for a comparative analysis of their biological activities with the other three taxa.

The biological targets chosen were diabetes (α -glucosidase inhibition test) and oxidative stress (DPPH, ABTS⁺, ORAC, and Folin-Ciocalteu tests). We also chose to focus, when available, on different plant parts: roots, branches, stems, leaves, flowers, and fruits.

Finally, a phytochemical study of the leaves of the taxon *V.c.* var. *cereum* was conducted to identify the secondary metabolites present in the ethanolic extract.



Sampling was performed between December 2014 and August 2016, with 53

- Seven samples of *Vaccinium cereum* var. *adenandrum* were collected on the island

- Samples from the different plant parts of these taxa were extracted by maceration

Table 3 details the obtained results. The yields of the crude extracts vary from 3–26% based on the initial dry matter mass. The mass yield of ethanolic extracts from leaves is the highest, with an average of 20%, those from fruits vary from 4–25% yield and those from roots vary from 3–17%.

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Taxon	Plant part	Sample name	Location	Date	Yield extract (%)	Inhibition of α -glucosidase	
						α -glucosidase inhibition at 10 μ g/mL ¹	IC ₅₀ of α -glucosidase in μ g/mL ²
<i>V.c. var. adenandrum</i>	Branches	Vca B	Fatu Hiva	December 14	9	98.8 $\pm$ 0.6	2.1 $\pm$ 0.7
	Sheets	Vca Fe1	Fatu Hiva	December 14	16.3	96.9 $\pm$ 0.5	5.3 $\pm$ 0.4
		Vca Fe2	Fatu Hiva	July 16	16.2	74.9 $\pm$ 7.1	4.5 $\pm$ 1.0
		Vca Fe3	Fatu Hiva	July 16	19.3	95.7 $\pm$ 1.9	0.9 $\pm$ 0.2
	Green fruits	Vca Gf	Fatu Hiva	December 14	4.4	100.0 $\pm$ 0.1	3.1 $\pm$ 0.9
	Roots	Vca R	Fatu Hiva	December 14	17.4	99.6 $\pm$ 0.2	0.7 $\pm$ 0.1
	Stems	Vca S	Fatu Hiva	December 14	14.8	99.7 $\pm$ 0.2	5.4 $\pm$ 0.2
<i>V.c. var. cereum</i>	Branches	Vcc B2	Tahiti – Aorai	February 15	4.1	100.0 $\pm$ 0.2	2.5 $\pm$ 0.4
		Vcc B3	Tahiti – Aorai	June 15	8.4	99.0 $\pm$ 0.5	1.4 $\pm$ 0.5
		Vcc B4	Tahiti – Aorai	June 15	5.3	98.9 $\pm$ 0.7	1.2 $\pm$ 0.4
		Vcc B5	Tahiti – Aorai	June 15	8.8	99.1 $\pm$ 0.6	1.0 $\pm$ 0.1
	Sheets	Vcc Fe1	Tahiti – Aorai	November 14	17.5	97.3 $\pm$ 0.2	6.1 $\pm$ 0.5
		Vcc Fe3	Tahiti – Aorai	June 15	15.1	97.3 $\pm$ 0.3	3.8 $\pm$ 0.5
		Vcc Fe4	Tahiti – Aorai	June 15	19.1	96.8 $\pm$ 0.5	5.0 $\pm$ 0.6
		Vcc Fe5	Tahiti – Aorai	June 15	17.4	96.8 $\pm$ 0.5	3.9 $\pm$ 0.6
		Vcc JFe6	Tahiti – Aorai	June 15	18.6	95.5 $\pm$ 0.6	7.2 $\pm$ 1.0
		Vcc Fe7	Tahiti – Marau	July 15	11.1	96.5 $\pm$ 0.4	7.2 $\pm$ 0.2
		Vcc Fe8	Tahiti – Marau	July 15	13.5	98.9 $\pm$ 0.3	4.0 $\pm$ 0.5
		Vcc Fe9	Tahiti – Marau	July 15	16.7	97.3 $\pm$ 1.2	4.1 $\pm$ 1.0
		Vcc Fe10	Tahiti – Aorai	July 16	20.1	95.7 $\pm$ 1.2	1.3 $\pm$ 0.2
		Vcc Fe11	Tahiti – Aorai	July 16	28.9	97.8 $\pm$ 0.2	0.7 $\pm$ 0.1
	Flowers	Vcc Fl1	Tahiti – Aorai	November 14	12.4	55.8 $\pm$ 5.9	9.8 $\pm$ 0.2
		Vcc Fl3	Tahiti – Aorai	June 15	16.8	98.6 $\pm$ 0.3	8.1 $\pm$ 0.3
		Vcc Fl6	Tahiti – Aorai	June 15	11	98.7 $\pm$ 0.4	7.6 $\pm$ 0.4
	Fruits	Vcc Fr1	Tahiti – Aorai	November 14	22.3	76.8 $\pm$ 1.3	8.8 $\pm$ 0.1
		Vcc Fr2	Tahiti – Aorai	February 15	5	58.4 $\pm$ 2.6	9.6 $\pm$ 0.1
		Vcc Fr3	Tahiti – Aorai	June 15	25.5	98.2 $\pm$ 0.4	7.8 $\pm$ 0.2
		Vcc Fr6	Tahiti – Aorai	June 15	21.5	86.6 $\pm$ 1.6	8.6 $\pm$ 0.1
		Vcc Fr9	Tahiti – Marau	July 15	10.3	4.7 $\pm$ 0.8	ND
	Green fruits	Vcc Frv9	Tahiti – Marau	July 15	3.2	36.3 $\pm$ 2.2	ND
	Roots	Vcc R2	Tahiti – Aorai	February 15	5.3	99.0 $\pm$ 0.4	0.8 $\pm$ 0.1
		Vcc R7	Tahiti – Marau	July 15	3	98.6 $\pm$ 0.5	1.1 $\pm$ 0.4
	Stems	Vcc T1	Tahiti – Aorai	November 14	11.5	98.8 $\pm$ 1.2	2.3 $\pm$ 0.3

Taxon	Plant part	Sample name	Location	Date	Yield extract (%)	Inhibition of α -glucosidase	
						α -glucosidase inhibition at 10 $\mu\text{g/mL}$ ¹	IC ₅₀ of α -glucosidase in $\mu\text{g/mL}$ ²
<i>V.c. var. cereum</i>	Stems	Vcc T3	Tahiti – Aorai	June 15	16.6	98.1 $\pm$ 0.9	3.7 $\pm$ 0.5
		Vcc T4	Tahiti – Aorai	June 15	11.6	98.3 $\pm$ 0.7	1.3 $\pm$ 0.3
		Vcc T5	Tahiti – Aorai	June 15	14.2	97.9 $\pm$ 1.4	3.0 $\pm$ 0.7
		Vcc T6	Tahiti – Aorai	June 15	16.7	99.5 $\pm$ 0.3	5.6 $\pm$ 0.4
		Vcc T7	Tahiti – Marau	July 15	4.7	100.0 $\pm$ 0.1	1.0 $\pm$ 0.2
		Vcc T8	Tahiti – Marau	July 15	4.4	100.0 $\pm$ 0.4	1.1 $\pm$ 0.2
		Vcc T9	Tahiti – Marau	July 15	2.8	98.9 $\pm$ 0.6	2.9 $\pm$ 0.4
<i>V.c. var. pubiflorum</i>	Branches	Vcp B	Tahiti – Orohena	July 15	7.7	99.8 $\pm$ 0.1	1.7 $\pm$ 0.9
	Sheets	Vcp Fe	Tahiti – Orohena	July 15	26.2	98.8 $\pm$ 0.2	2.9 $\pm$ 0.7
		Vcp Fe1	Tahiti – Aorai	August 16	26.3	100.0 $\pm$ 0.2	1.3 $\pm$ 0.1
		Vcp Fe2	Tahiti – Aorai	August 16	25.1	99.4 $\pm$ 0.2	0.8 $\pm$ 0.1
		Vcp Fe3	Tahiti – Aorai	August 16	22.2	99.6 $\pm$ 0.1	1.1 $\pm$ 0.2
	Flowers	Vcp Fl	Tahiti – Orohena	July 15	14.7	97.6 $\pm$ 0.4	7.9 $\pm$ 0.3
	Fruits	Vcp Fr	Tahiti – Orohena	July 15	17	96.8 $\pm$ 0.2	7.9 $\pm$ 0.3
	Roots	Vcp R	Tahiti – Orohena	July 15	7.3	99.7 $\pm$ 0.6	0.7 $\pm$ 0.1
	Stems	Vcp T	Tahiti – Orohena	July 15	9	99.4 $\pm$ 0.3	2.4 $\pm$ 0.3
<i>V.c. var. raiateense</i>	Sheets	Vcr Fe1	Raiatea	August 16	22.3	98.7 $\pm$ 0.1	0.6 $\pm$ 0.1
		Vcr Fe2	Raiatea	August 16	35	98.1 $\pm$ 0.2	1.2 $\pm$ 0.1
		Vcr Fe3	Raiatea	August 16	18.1	97.8 $\pm$ 0.2	0.5 $\pm$ 0.0
		Vcr Fe4	Raiatea	August 16	18.4	98.4 $\pm$ 0.2	1.4 $\pm$ 0.2

¹: α -glucosidase inhibition of acarbose at 300 $\mu\text{g/mL}$ = 56.7 $\pm$ 4.21%; ²: IC₅₀ of acarbose = 270.5 $\pm$ 3.73 $\mu\text{g/mL}$; ND: not determined.

Table 3.

Inhibitory potential of α -glucosidase of ethanolic extracts of *Vaccinium cereum* taxa.

9.6 $\mu\text{g/mL}$. These activities are very significant compared to that of the reference product used here and marketed in therapeutics, acarbose, which has an IC₅₀ of 270.5 $\mu\text{g/mL}$.

Figure 3 represents the average IC₅₀ on α -glucosidase obtained for the different plant parts of *Vaccinium cereum* taxa. The crude extracts of roots, branches, and stems have the highest activity toward α -glucosidase inhibition with mean IC₅₀ of 0.8 $\pm$ 0.2 $\mu\text{g/mL}$; 1.7 $\pm$ 0.6 $\mu\text{g/mL}$; and 2.7 $\pm$ 1.3 $\mu\text{g/mL}$, respectively. Leaves have intermediate activity with an average IC₅₀ of 4.9 $\pm$ 1.5 $\mu\text{g/mL}$.

The activity of the crude flower and fruit extracts was weaker, with average IC₅₀ of 8.4 $\pm$ 1.0 $\mu\text{g/mL}$ and 8.2 $\pm$ 0.9 $\mu\text{g/mL}$, respectively. These activities are still interesting compared to the inhibitory potential of acarbose (IC₅₀ of 270.5 $\pm$ 3.73 $\mu\text{g/mL}$).

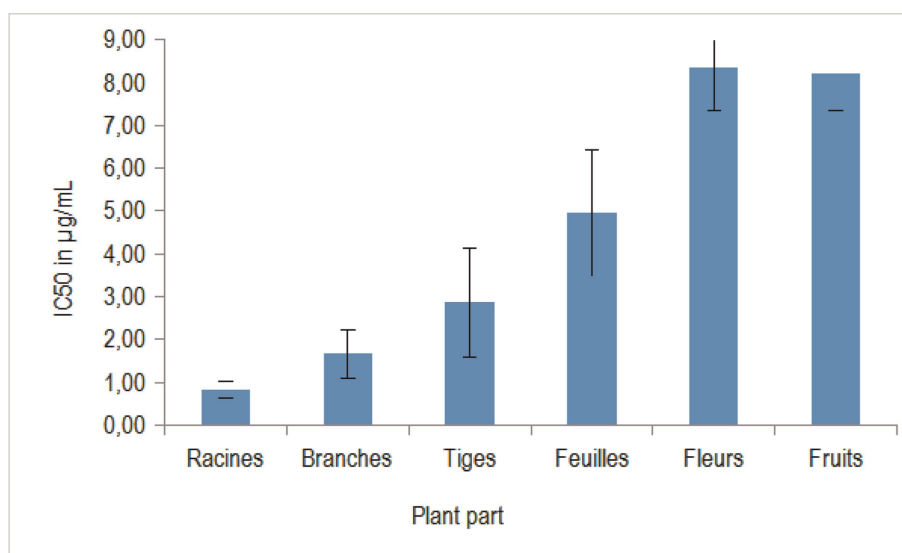


Figure 3.
 Graphical representation of the average IC₅₀ of extracts from different plant parts of *Vaccinium cereum* taxa on α -glucosidase. N = 4 for roots (Racines), 6 for branches (branches), 10 for stems (Tiges), 21 for leaves (Feuilles), 4 for flowers (Fleurs) and 8 for fruits (fruits).

Figure 4 represents the average IC₅₀ of leaf extracts for the four *Vaccinium cereum* taxa present in French Polynesia.

Thus, the average IC₅₀ of the leaves of *pubiflorum* and *raiateense* varieties appear to be the lowest with 1.5 µg/mL and 0.9 µg/mL, respectively. In contrast, the IC₅₀ of the varieties *adenandrum* and *cereum* vary from 0.9 to 5.3 µg/mL, and from 0.7 to 7.2 µg/mL, respectively, and show less inhibition compared to the other two varieties.

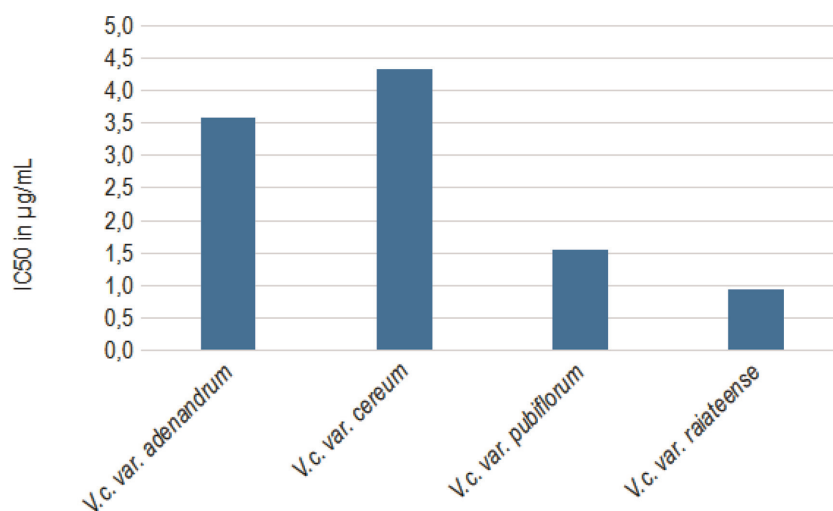


Figure 4.
 Graphical representation of the average IC₅₀ of leaf extracts of different *Vaccinium cereum* taxa on α -glucosidase. N = 3 for V.c. var. adenandrum, 10 for V.c. var. cereum, 4 for V.c. var. pubiflorum and 4 for V.c. var. raiateense.

The study of the antioxidant and antiradical potential was also carried out on the 53 samples of *V. cereum*. For this purpose, different complementary methods were used, namely:

- The radical recombination test to evaluate the antiradical potential of the extracts (two radicals tested: ABTS^{•+} and DPPH);
- The determination of total polyphenols by the Folin-Ciocalteu method allows to estimate the quantity of polyphenols present in the extracts. The correlation of this assay with the radical recombination test (DPPH and ABTS^{•+}) allows to know if the observed antiradical activity is associated with the presence of polyphenols in the extracts, and;
- The measurement of the ORAC index, allowing to evaluate the antioxidant capacity of the extracts.

The results obtained are presented in the following figures.

The EC₅₀ of the recombination of ethanolic extracts with DPPH vary from 71.4 µg/mL to 5.5 µg/mL for the most active extracts. The highest activity is observed for root and branch extracts with average EC₅₀ of 5.8 µg/mL and 8.4 µg/mL, respectively.

The same distribution of recombination activities is obtained with ABTS^{•+}, with root extracts again being the lowest EC₅₀ (3.6 µg/mL and 4.3 µg/mL, respectively) and therefore showing the highest potential (Figure 5).

The EC₅₀ on recombination with DPPH of leaf extracts from the four *V. cereum* taxa varied only slightly from 18.6 to 24.8 µg/mL. In contrast, the average EC₅₀ on ABTS^{•+} of leaf extracts of the varieties *raiateense* and *pubiflorum*, 4.8 and 6.9 µg/mL, is lower than that of leaf extracts of the varieties *adenandrum* and *cereum*, 12.0 and 14.6 µg/mL, respectively (Figure 6).

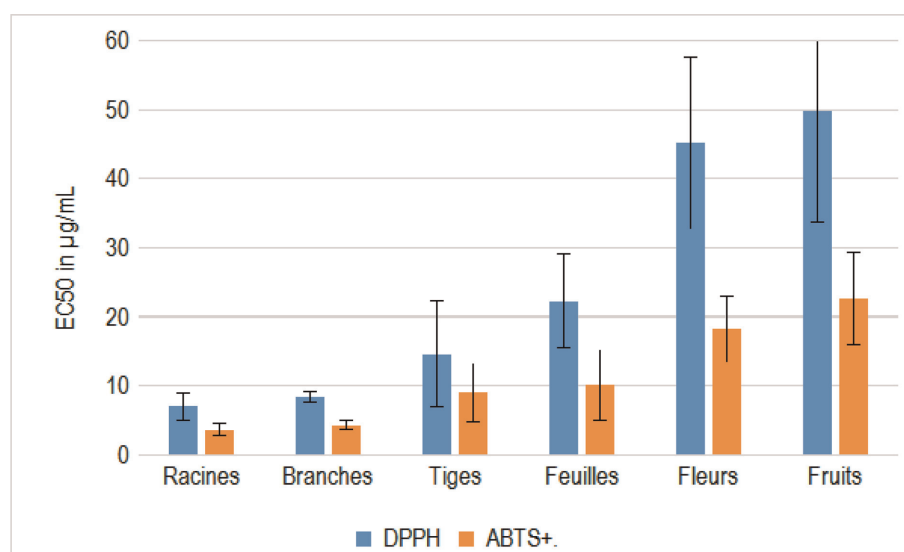


Figure 5.

Histogram of the average EC₅₀ of the extracts of the different plant parts of *Vaccinium cereum* taxa on the recombination of DPPH and ABTS^{•+} Radicals. N = 4 for roots (Racines), 6 for branches (branches), 10 for stems (Tiges), 21 for leaves (Feuilles), 4 for flowers (Fleurs) and 8 for fruits (fruits).

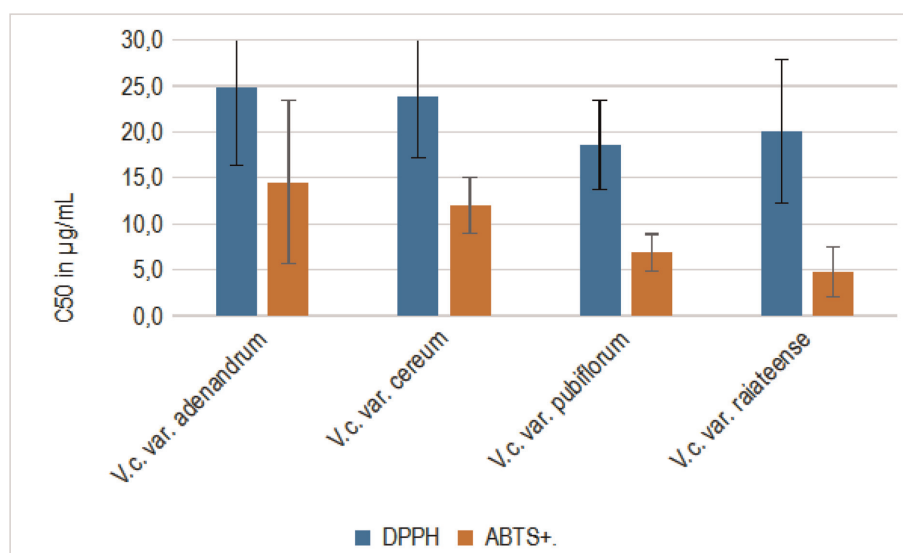


Figure 6.
 Histogram of the average EC_{50} of leaf extracts of the four *Vaccinium cereum* taxa on the recombination of DPPH and $ABTS^{+}$ Radicals. $N = 3$ for *V.c. var. adenandrum*, 10 for *V.c. var. cereum*, 4 for *V.c. var. pubiflorum* and 4 for *V.c. var. raiateense*.

For the Folin-Ciocalteu assay, all samples were assayed and the results obtained are expressed as catechin equivalent and gallic acid equivalent per 100 g of extract (expressed as percentage).

Thus, all samples contain polyphenols, but there are large differences with values ranging from 2.4% in catechin equivalent for the fruit extract of *V.c. var. cereum* (Vcc Fr2) to 89% in catechin equivalent for the root extract of *V.c. var. pubiflorum* (VcpR). Roots and stems are the plant parts containing the most polyphenols while fruits show a low concentration (Figure 7). However, the latter is described to be rich in anthocyanosides. The Folin-Ciocalteu method, although widely used, does not allow an accurate determination of polyphenols because the reagent is sensitive to any type of reductants (such as oses, proteins, etc.) [23].

The leaves of *V.c. var. raiateense* and *pubiflorum* are the richest in polyphenols with an average percentage of 42% and 37% in catechin equivalent. The least rich in polyphenols are the varieties *cereum* and *adenandrum*, with average percentages of 28% and 24% in catechin equivalent (Figure 8).

The ORAC antioxidant potential of all extracts was measured, the results obtained are expressed in $\mu\text{mol trolox equivalent/mg}$ of extract. All samples have a good antioxidant capacity with values ranging from 11.6 $\mu\text{mol trolox equivalent/mg}$ for the most active extract to 1.2 $\mu\text{mol trolox equivalent/mg}$ extract. These values confirm the strong antioxidant potential of *V. cereum* compared to the vitamin C index whose value is equal to 9.4 $\mu\text{mol trolox equivalent/mg}$.

All the extracts from the different parts of the plants seem to have the same antioxidant power (Figure 9), without any distinction being made on the ORAC index, especially for the leaves of the four taxa (Figure 10).

Vaccinium cereum is a wild shrub not cultivated in French Polynesia. The different taxa of *Vaccinium cereum* showed a very strong biological potential on the different biological targets chosen. The objective being to valorize this plant as a food

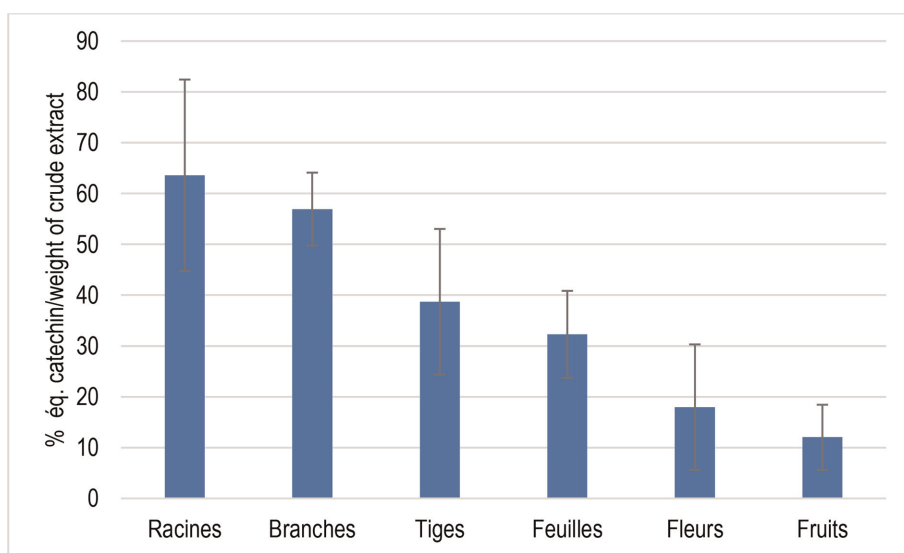


Figure 7.

Average percentage of total polyphenols in the crude extracts of the four *Vaccinium cereum* taxa. *N* = 4 for roots (Racines), 6 for branches (Branches), 10 for stems (Tiges), 21 for leaves (Feuilles), 4 for flowers (Fleurs) and 8 for fruits (Fruits).

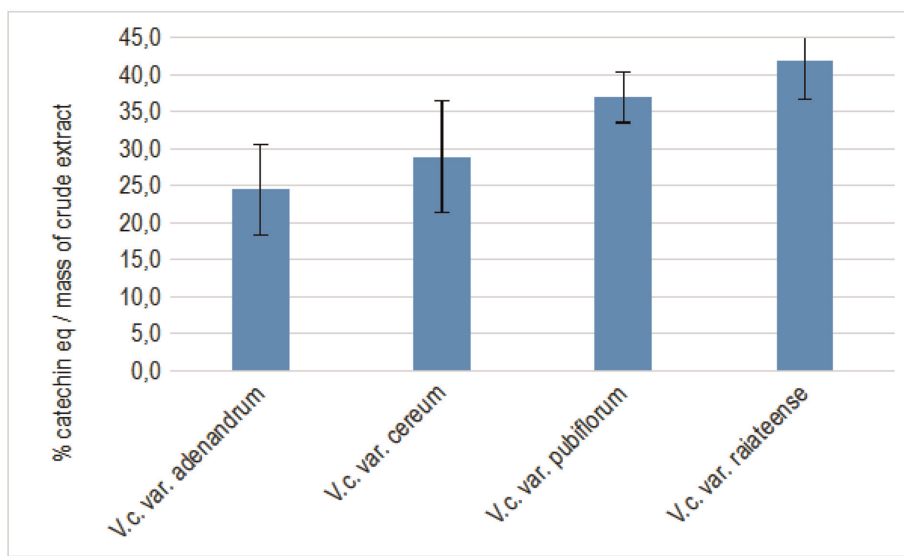


Figure 8.

Average percentage of total polyphenols in crude extracts of *Vaccinium cereum* leaves. *N* = 3 for V.c. var. adenandrum, 10 for V.c. var. cereum, 4 for V.c. var. pubiflorum and 4 for V.c. var. raiaiteense.

supplement to control glycemia, a phytochemical study was necessary to identify the secondary metabolites.

Among the taxa studied, *Vaccinium cereum* var. *cereum*, the most available and accessible, was chosen for this phytochemical study. Moreover, the evaluation of the inhibitory activity of α – glucosidase showed that all plant parts had a strong

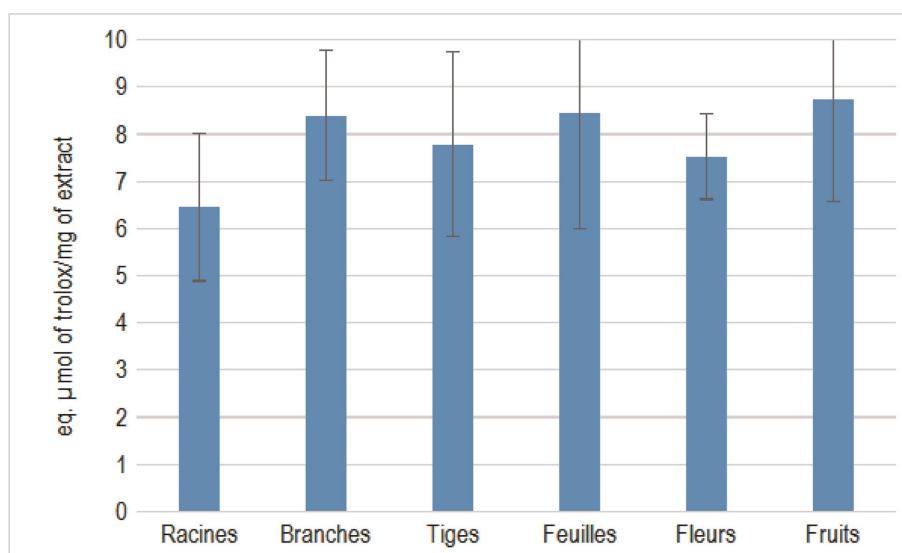


Figure 9.
 Average ORAC index of extracts from the different plant parts of the four *Vaccinium cereum* taxa. $N = 4$ for roots (Racines), 6 for branches (Branches), 10 for stems (Tiges), 21 for leaves (Feuilles), 4 for flowers (Fleurs) and 8 for fruits (Fruits).

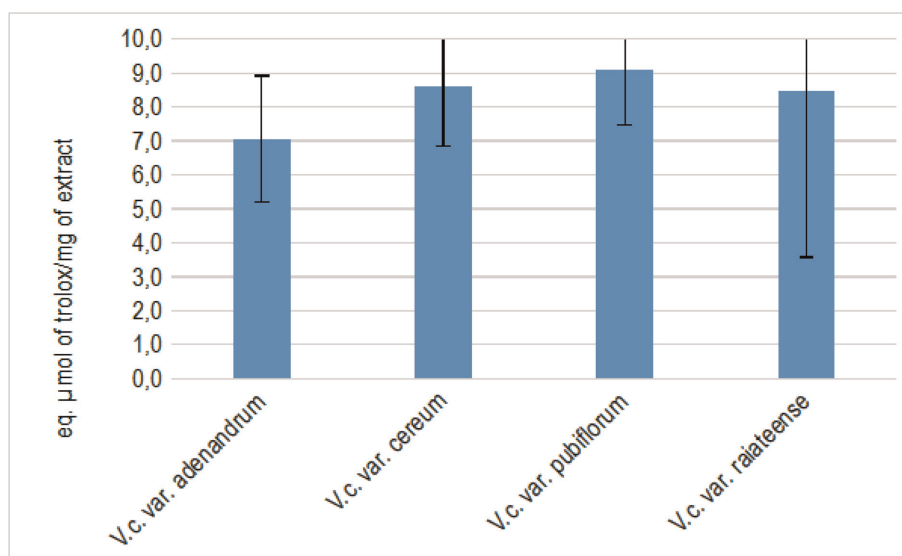


Figure 10.
 Average ORAC index of leaf extracts of the four *Vaccinium cereum* taxa. $N = 3$ for V.c. var. adenandrum, 10 for V.c. var. cereum, 4 for V.c. var. pubiflorum and 4 for V.c. var. raiaiteense.

inhibitory potential with low IC_{50} , lower than acarbose, the positive control. However, analysis of the data revealed a higher activity for roots and branches.

However, we chose to work on the leaves of *Vaccinium cereum* var. *cereum* because they show high activity, interesting extraction yield, and better availability (renewable resource).

2.3 Study and identification of secondary metabolites isolated from leaves of *Vaccinium cereum* var. *cereum*

The taxon was collected in November 2014 on Mount Aorai, Tahiti Island, Society Archipelago.

The dry powder of *V. c.* var. *cereum* leaves was macerated in 96% ethanol at room temperature. The resulting crude extract (SB02) was taken up in distilled water and then fractionated using liquid-liquid partitioning by solvents of increasing polarity: cyclohexane, dichloromethane, ethyl acetate, and butanol. The four organic phases and the residual aqueous phase were then concentrated to dryness (**Figure 11**).

Screening for α -glucosidase inhibition was performed. The crude extract as well as the phases from liquid/liquid partitioning, showed activities above 80% inhibition of the enzyme at a concentration of 10 μ g/mL.

The fractionation of the dichloromethane phase allowed the identification of two major compounds (Vc1 and Vc2).

The ethyl acetate phase led to the isolation of four compounds (Vc3 to Vc6).

2.3.1 Molecules isolated from the dichloromethane phase

2.3.1.1 Vc1 compound

A white amorphous powder was obtained, consisting of 95% of compound Vc1. The proton NMR of this compound is complex in the 0.5 to 2.5 ppm region and is characteristic of highly saturated compounds such as triterpenes with structures close to ursolic acid (**Figure 12** and **Table 4**).

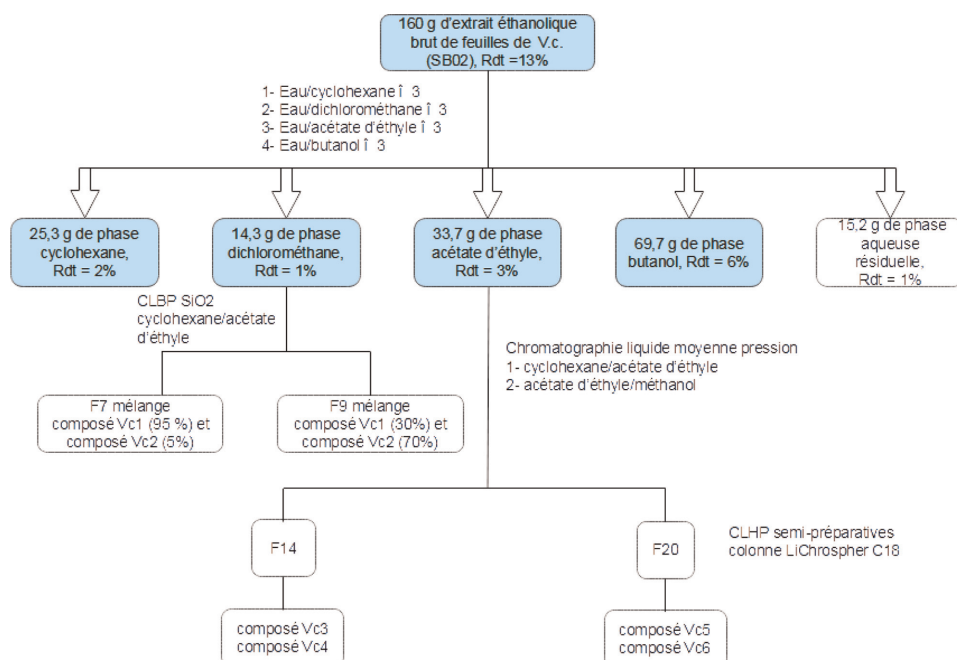


Figure 11.
Fractionation of the extract of leaves of *Vaccinium cereum* var. *cereum*.

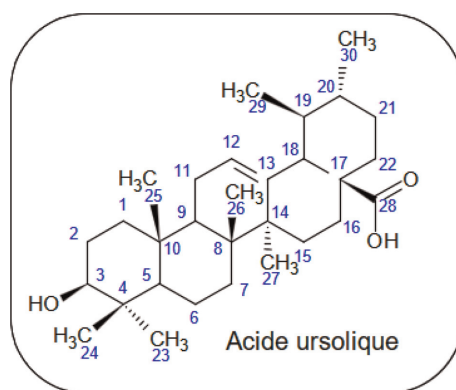


Figure 12.
Molecular structure of ursolic acid (*Acide ursolique*) extract from leaves of *Vaccinium cereum* var. *cereum*.

Compound Vc1: Ursolic acid		
	Experimental data	Literature [24]
Position	$\delta^1\text{H}$ (ppm, CD ₃ OD)	$\delta^1\text{H}$ (ppm, CDCl ₃)
3	3.16 (1H, dd, J = 11.5 and 4.3 Hz)	3.21 (1H, dd, J = 4.4 Hz and 10.2 Hz)
12	5.23 (1H, t, J = 3.9 Hz)	5.28 (1H, t, J = 3.6 Hz)
18	2.20 (1H, d, J = 11.5 Hz)	2.18 (1H, d, J = 11.7 Hz)
23	1.29 (3H, s)	1.25 (3H, s)
24	0.96 (3H, s)	0.98 (3H, s)
25	0.78 (3H, s)	0.77 (3H, s)
26	0.98 (3H, s)	1.08 (3H, s)
27	1.12 (3H, s)	1.14 (3H, s)
29	0.88(3H, d, J = 6.5 Hz)	0.93 (3H, d, J = 6.5 Hz)
30	0.96(3H, d, J = 4.5 Hz)	0.91 (3H, d, J = 5.9 Hz)

Table 4.
Comparison of NMR data ¹H of compound Vc1 and ursolic acid.

A triplet at 5.23 ppm is characteristic of the trisubstituted ethylenic group (H12) and coupled to two protons. The doublet at 2.20 ppm can be attributed to the proton carried by a tertiary carbon in α of a double bond and coupled to a single proton. Finally, in the area from 0.7 to 2.5 ppm five singlets and two doublets can be distinguished, proving the presence of 7 methyl groups. This skeleton would be that of ursolic acid (the spectra being recorded in MeOD, the proton of the acid function could not be distinguished).

The purity of the compound was measured at 95% by integration of the methyl signal at position 26. The IC₅₀ of the mixture with 95% of this compound was determined for α -glucosidase and was $10.9 \pm 0.9 \mu\text{g/mL}$, proving significant activity compared with the control acarbose (270.5 $\mu\text{g/mL}$).

Ursolic acid is present in many plants and found in other species of the genus *Vaccinium* such as *V. myrtillus*, *Vaccinium macrocarpon*, *V. oxycocos*, *Vaccinium angustifolium* and *Vaccinium vitis-idaea* [25–28].

Ursolic acid is known to have several pharmacological uses including anticancer of breast [29], liver [30], colon [31], prostate [26], blood [32], antioxidant [33], anti-inflammatory [34], antifilarial [35], hypolipidemic and liver-protective [36].

2.3.2 Vc2 compound

Compound Vc2 is a white amorphous powder. The proton NMR of this compound as for compound 1 is complex in the 0.5 to 2.5 ppm area and characteristic of highly saturated compounds like triterpenes (**Table 5**).

The presence of a triplet at 5.24 ppm is characteristic of the trisubstituted ethylenic group (H12) coupled to two protons. The split doublet at 2.85 ppm can be attributed to the proton carried by a tertiary carbon in α of a double bond and coupled to two protons. Finally, in the area from 0.7 to 2.5 ppm seven singletons can be distinguished, proving the presence of 7 methyl groups. This skeleton would be

Compound Vc2: Oleanolic acid		
	Experimental data	Literature [24]
Position	δ 1H (ppm, CD ₃ OD)	δ 1H (ppm, CDCl ₃)
3	3.15 (1H, dd, J = 11.4 and 4.3. Hz)	3.21 (1H, dd, J = 4.4 Hz and 10.2 Hz)
12	5.24 (1H, t, J = 4.7 Hz)	5.24 (1H, t, J = 3.6 Hz)
18	2.85 (1H, dd, J = 13.6 and 4.3 Hz)	2.82 (1H, dd, J = 4.3 Hz and 12.7 Hz)
23	0.98 (3H, s)	0.96 (3H, s)
24	0.78 (3H, s)	0.78 (3H, s)
25	0.82 (3H, s)	0.84 (3H, s)
26	0.75 (3H, s)	0.76 (3H, s)
27	1.29 (3H, s)	1.25 (3H, s)
29	0.85 (3H, s)	0.87 (3H, s)
30	0.91 (3H, s)	0.93 (3H, s)

Table 5.
Comparison of NMR data1 H of compound Vc2 and oleanolic acid.

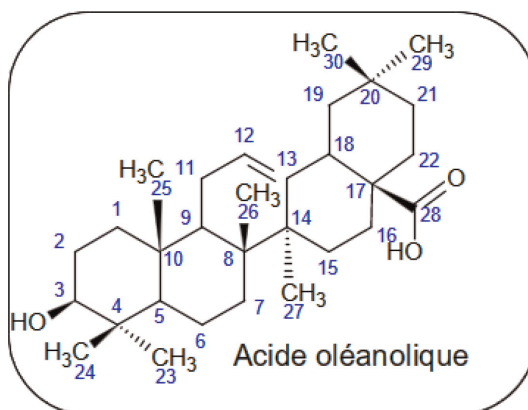


Figure 13.
Molecular structure of oleanolic acid (Acide ursolique) extract from leaves of *Vaccinium cereum* var. *cereum*.

that of the oleanolic acid (**Figure 13**). However, the spectra being recorded in MeOD, the proton of the acid function could not be distinguished.

The purity of the compound was measured at 70% by integrating the signal from the methyl at position 26 (CH₃). The IC₅₀ of the mixture with 70% of this compound was determined for α -glucosidase and is 4.2 ± 0.2 μ g/mL.

As ursolic acid, oleanolic acid is also present in many plants and found in other species of the genus *Vaccinium* such as *Vaccinium myrtillus*, *Vaccinium macrocarpon*, *V. oxycocos*, *Vaccinium angustifolium* and *Vaccinium vitis-idaea* [25–28].

Oleanolic acid also has several biological activities, such as anti-HIV [37], anticancer prostate [26], liver [30], antioxidant [38], anti-inflammatory [34], hepatoprotective [39] and hypolipidemic [36].

2.3.3 Molecules isolated from the ethyl acetate phase

2.3.3.1 Vc3 compound

The compound Vc3 is a yellowish solid. It has a UV spectrum characteristic of caffeoylquinic acids ($\lambda_{\text{max}} \approx 296$ and 326 nm) [40]. The proton and carbon NMR of this compound confirms that it is the methyl ester form of chlorogenic acid with the presence of a methyl at 3.69 ppm and an observed HMBC correlation of this CH₃ with C-7 at 174.0 ppm (**Figure 14** and **Table 6**) [41, 42].

2.3.3.2 Vc4 compound

The compound Vc4 is a yellowish solid. It has a UV spectrum characteristic of caffeoylquinic acids ($\lambda_{\text{max}} \approx 296$ and 326 nm) [40]. The proton and carbon NMR of

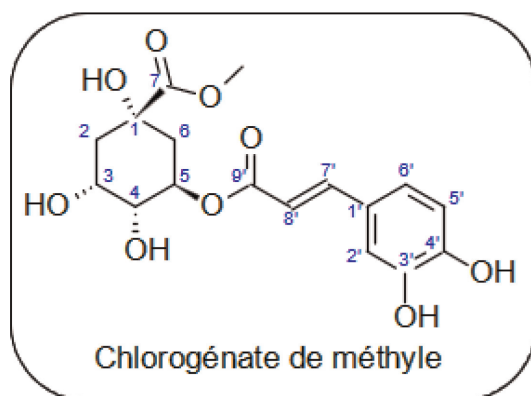


Figure 14.
Molecular structure of methyl chlorogenate (*Chlorogénate de méthyle*) isolated from leaves of *Vaccinium cereum* var. *cereum*.

Compound Vc3: Methyl chlorogenate or methyl ester of 5-O (E)-caffeoylquinic acid				
	Experimental data		Literature [41]	
Position	$\delta^1\text{H}$ (ppm, CD ₃ OD)	$\delta^1\text{H}$ (ppm, CD ₃ OD)	$\delta^{13}\text{C}$ (ppm, CD ₃ OD)	$\delta^{13}\text{C}$ (ppm, CD ₃ OD)
1			74.5	74.5

Compound Vc3: Methyl chlorogenate or methyl ester of 5-O (E)-caffeoylquinic acid				
	Experimental data	Literature [41]	Experimental data	Literature [41]
2a	2.20 (1H, m)	2.16 (1H, dd, J = 3.8 Hz and 12.3 Hz)	36.6	36.4
2b	2.14 (1H, m)	2.00 (1H, m)	36.6	36.4
3	4.14 (1H, m)	4.17 (1H, m)	68.9	69.0
4	3.74 (1H, m)	3.73 (1H, dd, J = 2.8 Hz and 7.4 Hz)	70.7	70.8
5	5.28 (1H, m)	5.27 (1H, td, J = 4.5 Hz and 7.4 Hz)	70.7	70.4
6a	2.20 (1H, m)	2.21 (1H, dd, J = 2.8 Hz and 12.3 Hz)	36.6	36.7
6b	2.02 (1H, dd, J = 6.2 and 12.5 Hz)	2.02 (1H, m)	36.6	36.7
7			174.0	174.1
1'			126.2	126.3
2'	7.05 (1H, s)	7.03 (1H, d, J = 1.9 Hz)	113.7	114.0
3'			145.4	145.6
4'			148.3	148.4
5'	6.78 (1H, d, J = 8.3 Hz)	6.78 (1H, d, J = 8.2 Hz)	115.2	115.2
6'	6.95 (1H, d, J = 8.3 Hz)	6.95 (1H, dd, J = 1.9 Hz and 8.2 Hz)	121.7	121.6
7'	7.52 (1H, d, J = 15.7 Hz)	7.52 (1H, d, J = 16.1 Hz)	145.8	145.9
8'	6.21 (1H, d, J = 15.7 Hz)	6.21 (1H, d, J = 16.1 Hz)	113.6	113.7
9'			166.9	166.9
O-CH3	3.69 (3H, s)	3.69 (3H, s)	51.7	51.6

Table 6.

Comparison of ^1H NMR and ^{13}C NMR data of Vc3 compound and methyl chlorogenate.

this compound is similar to that of compound Vc3, but the absence of the singlet at 3.69 ppm in ^1H NMR1 corresponding to the O-CH₃ of the ester indicates the presence of chlorogenic acid (**Figure 15** and **Table 7**) [43].

Both molecules Vc3 and Vc4 did not show α -glucosidase inhibitory activity at 10 $\mu\text{g/mL}$, but chlorogenic acid and its derivatives are known to have antioxidant [44], bactericidal [45], anti-inflammatory, analgesic, antipyretic [46] and anticancer properties by inhibiting carcinogenesis *in vivo* [47].

2.3.3.3 Vc5 compound

The compound Vc5 is a yellowish solid. The 5 aromatic protons H-6, H-8, H-2', H-3' and H-6', present in proton NMR, are characteristic of the quercetin skeleton (**Figure 16**). The presence of a doublet at 5.25 ppm integrating for a proton (anomeric proton) is characteristic of the presence of an O-glycosidic bond. The chemical shift of

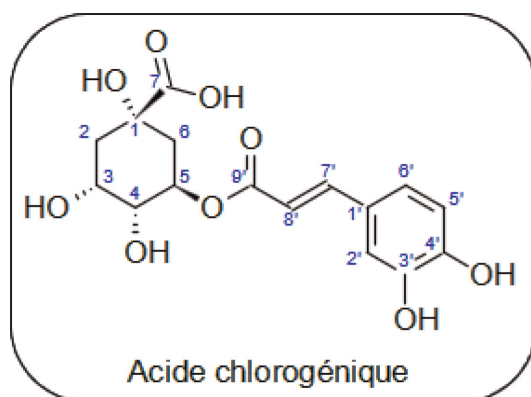


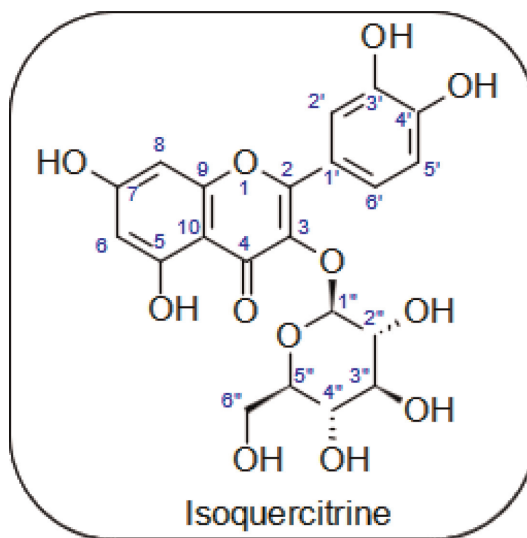
Figure 15.
 Molecular structure of chlorogenic acid (*Acide chlorogénique*) isolated from leaves of *Vaccinium cereum* var. *cereum*.

Compound Vc4: Chlorogenic acid or 5-O-caffeoylquinic acid				
	Experimental data	Bibliographic data	Experimental data	Literature [43]
Position	$\delta^1\text{H}$ (ppm, CD ₃ OD)	$\delta^1\text{H}$ (ppm, CD ₃ OD)	$\delta^{13}\text{C}$ (ppm, CD ₃ OD)	$\delta^{13}\text{C}$ (ppm, CD ₃ OD)
1			75.9	74.7
2a	2.18 (1H, m)	2.17 (1H, dd, J = 3.1 Hz and 14.1 Hz)	38.1	37.3
2b	2.16 (1H, m)	2.04 (1H, dd, J = 4.9 Hz and 14.1 Hz)	38.1	37.3
3	4.14 (1H, m)	4.14 (1H, ddd, J = 3.1 Hz; 3.3 Hz and 4.9 Hz)	70.5	70.5
4	3.74 (1H, dd, J = 2.7 Hz and 7.8 Hz)	3.71 (1H, dd, J = 3.3 Hz and 8.5 Hz)	72.3	72.1
5	5.28 (1H, ddd, J = 4.6 Hz; 7.8 Hz and 9.2 Hz)	5.31 (1H, ddd, J = 4.2 Hz; 8.5 Hz and 9.1 Hz)	72.3	70.6
6a	2.18 (1H, m)	2.14 (1H, dd, J = 4.2 Hz and 14.0 Hz)	38.1	36.8
6b	2.01 (1H, dd, J = 9.2 Hz and 13.7 Hz)	2.08 (1H, dd, J = 9.1 Hz and 14.0 Hz)	38.1	36.8
7			175.1	175.6
1'			127.7	126.4
2'	7.04 (1H, d, J = 2.1 Hz)	7.03 (1H, d, J = 1.9 Hz)	115.2	113.9
3'			146.9	145.3
4'			149.8	148.1
5'	6.78 (1H, d, J = 7.8 Hz)	6.75 (1H, d, J = 8.1 Hz)	116.6	115.1
6'	6.94 (1H, dd, J = 2.1 Hz and 7.8 Hz)	6.94 (1H, dd, J = 1.9 Hz and 8.1 Hz)	123.1	121.6
7'	7.53 (1H, d, J = 15.9 Hz)	7.56 (1H, d, J = 15.8 Hz)	147.3	145.7

Compound Vc4: Chlorogenic acid or 5-O-caffeoylquinic acid				
	Experimental data	Bibliographic data	Experimental data	Literature [43]
8'	6.22 (1H, d, J = 15.9 Hz)	6.22 (1H, d, J = 15.8 Hz)	115.1	113.8
9'			168.4	167.3

Table 7.

Comparison of ^1H NMR and ^{13}C NMR data of compound Vc4 and chlorogenic acid.

**Figure 16.**

Molecular structure of isoquercitrin (Isoquercitrine) isolated from leaves of *Vaccinium cereum* var. *cereum*.

Compound Vc5: quercitrin-3-O-glucoside or isoquercitrin				
	Experimental data	Bibliographic data	Experimental data	Literature [48]
Position	$\delta^1\text{H}$ (ppm, CD ₃ OD)	$\delta^1\text{H}$ (ppm, CD ₃ OD)	$\delta^{13}\text{C}$ (ppm, CD ₃ OD)	$\delta^{13}\text{C}$ (ppm, CD ₃ OD)
2			159.1	159.2
3			135.8	135.8
4			179.6	179.6
5			163.1	163.2
6	6.20 (1H, d, J = 1.7 Hz)	6.20 (1H, s)	100.1	100.1
7			166.3	166.3
8	6.39 (1H, J = 1.7 Hz)	6.39 (1H, s)	94.9	94.9
9			158.7	158.6
10			105.8	105.8
1'			123.2	123.2

Compound Vc5: quercitrin-3-O-glucoside or isoquercitrin				
	Experimental data	Bibliographic data	Experimental data	Literature [48]
2'	7.71 (1H, d, J = 1.7 Hz)	7.70 (1H, s)	117.7	117.7
3'			146.1	146.1
4'			150.0	150.0
5'	6.87 (1H, d, J = 8.5 Hz)	6.87 (1H, d, J = 8.3 Hz)	116.2	116.1
6'	7.59 (1H, dd, J = 1.7 and 8.5 Hz)	7.58 (1H, d, J = 8.3 Hz)	123.2	123.3
1''	5.25 (1H, J = 7.5 Hz)	5.24 (1H, d, J = 7.6 Hz)	104.4	104.5
2''	3.48 (1H, J = 7.9 Hz)	3.48 (1H, t, J = 8.4 Hz)	75.8	75.9
3''	3.43 (1H, J = 8.9 Hz)	3.43 (1H, t, J = 8.9 Hz)	78.2	78.3
4''	3.35 (1H, J = 9.3 Hz)	3.35 (1H, t, J = 9.2 Hz)	71.3	71.4
5''	3.25 (1H, m)	3.22 (1H, m)	78.5	78.5
6 "a	3.58 (1H, dd, J = 5.4 and 11.6 Hz)	3.57 (1H, dd, J = 5.3 Hz and 11.8 Hz)	62.7	62.7
6 "b	3.71 (1H, dd, J = 2.1 and 11.6 Hz)	3.70 (1H, d, J = 11.8 Hz)	62.7	62.7

Table 8.
 Comparison of ^1H NMR and ^{13}C NMR data of compound Vc5 and isoquercitrin.

the carbons and protons are characteristic of glucose. Compound Vc5 is isoquercitrin (Table 8).

Isoquercitrin is a flavonoid found in various medicinal plants. The glycosylated derivative of quercetin would have a bioavailability superior to the aglycone. In addition to the antioxidant effect, it is attributed to various biological activities including antidiabetic, anti-inflammatory during allergic reactions, cardioprotective, and anticancer [49, 50].

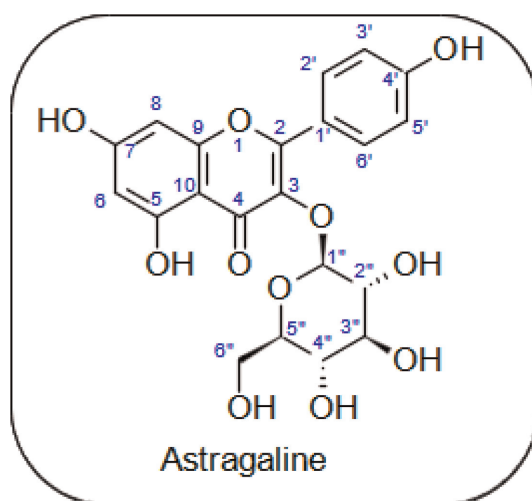


Figure 17.
 Molecular structure of astragalin (Astragaline) isolated from leaves of *Vaccinium cereum* var. *cereum*.

2.3.3.4 Vc6 compound

The compound Vc6 is a yellowish solid. The 6 aromatic protons H-6, H-8, H-2', H-3' H-5', and H-6', present in proton NMR, are characteristic of the kaempferol skeleton (**Figure 17**). The presence of a double at 5.24 ppm integrating for 1 H (anomeric proton) is characteristic of the presence of an O-glycosidic bond. The chemical shift of the carbons and protons is characteristic of glucose. The compound Vc6 is astragalin (**Table 9**).

Compound Vc6: Kaempferol-3-O-glucoside or astragalin				
	Experimental data	Bibliographic data	Experimental data	Literature [48]
Position	$\delta^1\text{H}$ (ppm, CD_3OD)	$\delta^1\text{H}$ (ppm, CD_3OD)	$\delta^{13}\text{C}$ (ppm, CD_3OD)	$\delta^{13}\text{C}$ (ppm, CD_3OD)
2			157.1	159.3
3			134	135.8
4			178.1	179.8
5			161.7	163.4
6	6.19 (1H, d, $J = 1.9$ Hz)	6.17 (1H, d, $J = 1.9$ Hz)	98.5	100.8
7			164.6	167.9
8	6.39 (1H, d, $J = 1.9$ Hz)	6.36 (1H, d, $J = 1.9$ Hz)	93.3	95.5
9			157.7	159.0
10			104.3	105.7
1'			121.36	123.2
2'	8.05 (1H, d, $J = 8.6$ Hz)	8.05 (1H, d, $J = 8.9$ Hz)	130.9	132.7
3'	6.88 (1H, d, $J = 8.6$ Hz)	6.88 (1H, d, $J = 8.9$ Hz)	114.7	116.5
4'			160.1	162.0
5'	6.88 (1H, d, $J = 8.6$ Hz)	6.88 (1H, d, $J = 8.9$ Hz)	114.7	116.5
6'	8.05 (1H, d, $J = 8.6$ Hz)	8.05 (1H, d, $J = 8.9$ Hz)	130.9	132.7
1''	5.25 (1H, d, $J = 7.3$ Hz)	5.22 (1H, d, $J = 7.6$ Hz)	102.6	104.7
2''	3.44 (1H, dd, $J = 7.3$ Hz and 9.3 Hz)	3.44 (1H, t, $J = 9.2$ Hz)	74.3	76.1
3''	3.42 (1H, t, $J = 9.1$ Hz)	3.41 (1H, t, $J = 9.2$ Hz)	76.6	78.5
4''	3.33 (1H, m)	3.31 (1H, t, $J = 9.8$ Hz)	69.9	71.8
5''	3.21 (1H, m)	3.19 (1H, m)	77.0	78.8
6 "a	3.53 (1H, dd, $J = 5.4$ Hz and 11.8 Hz)	3.53 (1H, dd, $J = 5.5$ Hz and 11.8 Hz)	61.2	63.0
6 "b	3.70 (1H, dd, $J = 2.2$ Hz and 11.8 Hz)	3.68 (1H, dd, $J = 2.4$ Hz and 11.8 Hz)	61.2	63.0

Table 9.
Comparison of ^1H NMR and ^{13}C NMR data of compound Vc6 and astragalin.

Astragalin is a flavonoid endowed with, in addition to its antioxidant effect, an anti-inflammatory activity on atopic dermatitis by acting on the inhibition of inflammation-inducing liposaccharide mediators [48, 51].

3. Conclusion

The study of *Vaccinium cereum* showed a very high interest in the inhibition of α -glucosidase, an enzyme involved in type 2 diabetes (T2DM).

All ethanolic crude extracts from the roots, branches, stems, leaves, flowers, and fruits of *V. c. var. cereum*, *V. c. var. pubiflorum*, *V. c. var. adenandrum* and *V. c. var. raiateense*, without exception inhibit this enzyme with low IC_{50} ranging from 0.5 to 9.6 $\mu\text{g/mL}$ compared to acarbose, the positive control used in the treatment of T2DM which inhibits the enzyme with an IC_{50} of 270.5 $\mu\text{g/mL}$.

The highest activities are observed for roots and branches of three endemic *Vaccinium cereum* taxa with average IC_{50} of 0.8 and 1.7 $\mu\text{g/mL}$, respectively.

In addition to α -glucosidase inhibitory activity, the extracts showed significant antioxidant and antiradical activities.

We were able to show a positive correlation between the α -glucosidase inhibition test and the antioxidant activities thanks to the accumulated data. The results suggest that the inhibitory activity of α -glucosidase is due in particular to the presence of polyphenols.

The phytochemical study of the leaves isolated and identified oleanolic acid and ursolic acid from the dichloromethane phase from the liquid-liquid partition of the ethanolic extract. Both acids showed a low IC_{50} of 10.9 and 4.2 $\mu\text{g/mL}$ on α -glucosidase, respectively, compared to acarbose which has an IC_{50} of 270.5 $\mu\text{g/mL}$. These two triterpene acids are present in species of the genus *Vaccinium* and have various activities as anticancer, hypolipidemic, hepatoprotective, and antidiabetic.

From the ethyl acetate phase, phenolic compounds were isolated and identified such as chlorogenic acid and its methyl ester, astragalin, and isoquercitrin. In addition to their strong antioxidant activity, these phenolic compounds have anti-inflammatory and antibiotic activities. Hydroxycinnamic acid derivatives are also present in this extract.

Therefore, all these results revealed that this taxon represents a real health benefit and might have promising proprieties to regulate blood sugar.

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