Fabiana punensis S.C. Arroyo, *F. bryoides* Phil., *F. densa* Remy, *F. patagonica* Speg.

María Inés Isla, Mariana Leal, Daniela González, Eugenia Orqueda, Iris Catiana Zampini, and Ana Soledad Cuello

(**a**) *F. punensis* (**b**) *F. bryoides*, (**c**) *F. densa* and (**d**) *F. patagonica,* from Argentine Puna. Antofagasta de la Sierra, Catamarca, Argentina. (Photos: S. Cuello and C. Zampini)

M. I. Isla (✉) · M. Leal · D. González · E. Orqueda · I. C. Zampini · A. S. Cuello
Instituto de Bioprospección y Fisiología Vegetal (INBIOFIV, CONICET- Facultad de Ciencias Naturales e Instituto Miguel Lillo-Universidad Nacional de Tucumán), San Miguel de Tucumán, Argentina
e-mail: misla@csnat.unt.edu.ar; zampini@csnat.unt.edu.ar

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Abstract *Fabiana* Ruiz & Pav. (Solanaceae) is a South American genus, growing especially in arid mountainous areas. In Argentina, 10 species are present in the High Andean, Pre-Puna, Puna, and Monte biogeographical regions, in addition to Patagonia. In this chapter reference is made to four *Fabiana* species, *F. punensis, F. patagonica, F. bryoides* and *F. densa.* They are described as medicinal plants under the common names of "tola" or "tolilla". Progress is reported regarding the scientific validation of medicinal properties, as well as the study of the chemical composition of these species. The potential as antioxidants, anti-inflammatory, and antibiotics agents from the hydroalcoholic or aqueous extracts from the aerial parts was described. Antioxidant and diuretic properties of infusions and essential oils was demonstrated. The safety of these preparations has also been demonstrated, although further *in vivo* studies would be necessary to fully demonstrate the safety of the extracts Presently, prolonged traditional use by local communities is still recognized to support their safe use. Studies are needed about the agronomic conditions for its cultivation so that these species could be used as raw material in phytotherapic and phytocosmetic preparations.

Keywords "Tola" · Argentine medicinal plant · Anti-inflammatory · Antibiotic · Antioxidant · Diuretic

1 Introduction

Fabiana is a native medicinal plant genus with several underutilized species, in Argentina. Four *Fabiana* species*, F. punensis, F. densa, F. bryoides,* and *F. punensis,* that grown in arid regions, have pharmacological properties and as such can be regarded as possible candidates for domestication. Also, as a raw material source for phytotherapic and phytocosmetic preparations they could be used to improve the quality of life.

2 Taxonomic Characteristics

Fabiana R. et P. is a South American genus of the Family Solanaceae that comprises 15 species, some present in Peru, Chile and Bolivia. In Argentina, inhabits the High Andean, Pre-Puna, Puna and Monte biogeographical regions, including in Patagonia (Cabrera 1957, 1968, 1983; Barboza and Hunziker 1993, 1998; Barboza and Romanutti 1999; Cuello 2006; Carilla et al. 2018). The largest number of species, are distributed in Argentina, 10 of the 15, with five endemic species (*F. friesii, F. nana, F. peckii, F. foliosa* and *F. punensis*), followed by Chile with two

(*F. squamata* and *F. viscosa*) and Bolivia with one (*F. fiebrigii*). Argentina shares the species *F. patagonica, F. densa* with Bolivia and *F. bryoides, F. imbricata* and *F. denudata* with Chile.

This genus was described by Hipólito Ruiz López and José Antonio Pavón and the name *Fabiana* is a tribute to Archbishop of Valencia, Spain, Francisco Fabián y Fuero (1719–1801), patron of botany. In this chapter reference will be made to four *Fabiana* species, *F. punensis, F. patagonica, F. bryoides* and *F. densa.*

While the genus *Fabiana* was described at the end of the 18th century, the species *F. punensis* S.C. Arroyo was known in Arroyo 1976, by Silvia Arroyo, from specimens collected in the department of Cochinoca, in the Puna from Jujuy. It is known under the common name of "tolilla" (Barboza and Hunziker 1993, 1998; Barboza and Romanutti 1999). *F. patagonica* Speg. popularly known as "tolilla", "checal" or "tola". *F. bryoides* Phil. is called "pata de perdíz" or "pata de loro" by the Puna people. And *F. densa* Rémy (The Plant List 2019), is known as "tolilla" or "checal" (Bolivia) (Barboza and Hunziker 1993, 1998) just like *F. patagonica*, The common name "tola o tolilla" is widely used by the inhabitants from Puna region to name the bushes. The word "tola" belongs to the Aymara language, which means strong, resistant, "who does not know diseases" and "tolilla" is the diminutive of the word "tola".

3 Crude Drug Used

In Argentina, traditional medicine uses the leaves, branches and flowers of the four *Fabiana* species described in this chapter. Generally, the plant material is dried and pulverized prior to use. In Fig. 1, the picture of aerial parts of each *Fabiana* species are illustrated. In the case of *F. densa*, the resinous exudate from the leaves, is used.

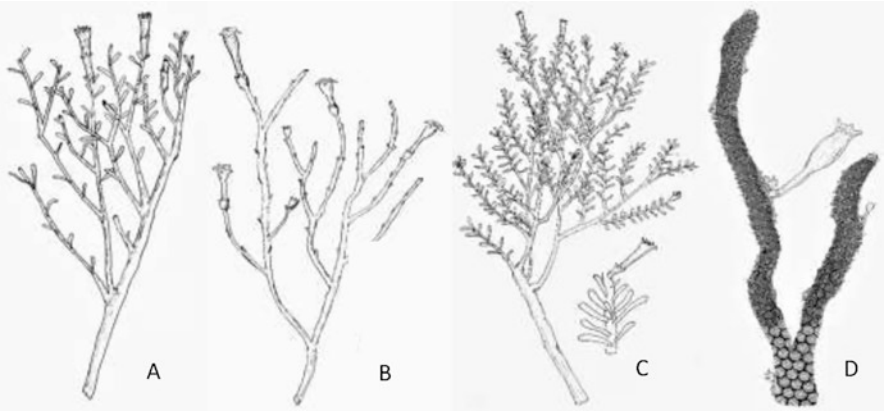

Fig. 1 Used parts for medicines of (**a**) *F. patagonica;* (**b**) *F. punensis;* (**c**) *F. densa*; (**d**) *F. bryoides*. (Pictures: M Leal)

4 Major Chemical Constituents and Bioactive Compounds

Fatty acids composition of seeds from *F. densa* and *F. punensis* was determined. Linoleic acid was dominant with 61.3 and 59.6% of the total fatty acids content to *F. densa* and *F. punensis*, respectively. Palmitic, and oleic acids constituting 13–16%. Other fatty acids (myristic, palmitoleic, linolenic, arachidonic, behenic and lignoceric) were also detected. Stigmasterol, sitosterol and *Z*~S-avenasterol were identified. Sitosterol was dominant in both species (around 50%). Cholesterol would be present in comparatively large quantities (0.4–14.4%) (Maestri and Guzmán 1995).

From the aerial parts of *F. densa* the following compounds have been isolated: two diterpenes, *ent*-beyer-15-en-18-*O*-succinate and *ent*-beyer-15-en-18-*O*-oxalate (Erazo et al. 2002) with antimicrobial activity. Recently the isolation and structural elucidation of other tetracyclic *ent*-beyerene diterpenes derivatives was reported. In addition to the succinoyl and the oxaloyl esters, the alcohol and the malonoyl ester were also isolated. Both diterpenes demonstrate a selective activity against Gram (+) bacterial strains with negligible cytotoxicity towards human keratinocytes (Quaglio et al. 2020). Triterpenes as ursolic and oleanolic acids were identified in *F. densa* (Quaglio et al. 2020).

Oleanolic acid was also isolated and identified in a *F. patagonica* infusion and could be a responsible factor of the diuretic activity demonstrated for this plant (Álvarez et al. 2002).

The ethanolic extracts of *F. punensis* and *F. patagonica* contain phenolic components, principally rutin (Cuello et al. 2011; Cuello 2012; Orqueda 2014). In aqueous extracts of *F. punensis* and *F. densa* were identified phenolic components. Chlorogenic acid and rutin were identified in *F. bryoides* and quercetin in *F. punensis* (Cuello et al. 2011; Cuello 2012). Chlorogenic acid is important member of hydroxycinnamic acid with natural antioxidant, cardioprotective, anti-Alzheimer, antidiabetic, anti-inflammatory properties and inhibits DNA damage (Agunloye et al. 2019).

The volatile fraction of *F. punensis* contains sesquithuriferol (29.4%), α-pinene (12.7%), β-pinene (11.5%) terpinen-4-ol (6.2%) as main compounds (Rodríguez et al. 2018).

5 Morphological Description

Fabiana punensis Shrub very resinous of 0.5–1.20 m high. Glabrescent branches, straight, with few alternate leaves as spatula, sessile, glabrous, deciduous. Sessile terminal flowers on very short braquiblasts. Tubular calyx, glabrous or barely glandulous-pubescent, cylindrical tube, short triangular apical lobes. Corolla tubular, white-yellowish color with violet base, hypocrateriform, glabrous, short lobes, patents, heterodynamic stamens, adhered to (3−) 4−6 (−7) mm from the base of the corolla, the 2 longer filaments of 6 to 8 mm (almost the same length as the corolla

tube) and 3 more 4–6 mm short, 1–1.2 × 0.3–0.5 mm anthers; obovoid ovary, 1.5–2 × 0.8–1 mm, 7−9 mm style, truncated stigma in the shape of a saddle. Obovoid capsule, 5−6 (−7) × 2−3 mm; globose or ellipsoid seeds, brown (Barboza and Hunziker 1993, 1998).

Fabiana bryoides Low shrubs of ± 50 cm high. Macroblasts that are often born from knots very close to each other, coated completely by braquiblasts with squamiform and glabrescent leaves. Lonely lowers in each braquiblast; calyx, urceolate tube, segments triangular; infundibuliform corolla with the tube quite thinned in its lower half; very small anthers (0.5–0.7 mm), almost as long as wide, confluent teak; semilunar stigma, just low cut. Capsule with small seeds (Barboza and Hunziker 1993, 1998.).

Fabiana densa Shrubs up to l m high, characteristic for its gemmiferous roots, the density of its foliage and the glandular pubescence. Flowers on macroblasts or braquiblasts; pedicels up to 4.5 mm; calyx 3–5.7 mm, urceolate tube at its base, 2.2–3.7 (4) mm, 1–2 mm segments, narrow-triangular or triangular; infundibuliform corolla, 10–13 (13.5) mm, often with stretch marks reddish or violet on a background yellowish; androecium heterodynamic, 0.7–1 mm anthers; chair-shaped stigma of mount. 6–7 mm capsule. Seeds 1.4–1.5 × 0.5–0.6 × 0.3 mm (Barboza and Hunziker 1993, 1998)

Fabiana patagonica Shrubs of 2 m high. Macroblasts straight or flexible. Leaves solitary or, in the apical branches, fasciculate on brachiblasts. Flowers lonely on brachiblasts, rare terminals on macroblasts; cylindrical tube, hypocraterimorph, with the straight tube that it ends in a subapical widening; androecium homodynamic, ellipsoid anthers, 0.8–1.4 × 0.6–1.3 mm, confluent teak, capitized stigma, something depressed. 6–8 mm capsule. Seeds 1.3–1.8 × 0.6–0.9 × 0.5 mm (Barboza and Hunziker 1993, 1998).

6 Geographical Distribution

The South American genus *Fabiana* (Solanaceae) grows along arid mountainous area between 16° and 51° S, between 1200 and 4900 m.a.s.l. There are 15 species in the region, ten are present in Argentina, seven in Chile, four in Bolivia and one in Peru. There are five species in the Altoandina, Puna, Pre-Puna and Monte phytogeographic regions of the Argentinean Northwest (Cabrera 1957, 1968, 1983; Barboza and Hunziker 1993, 1998; Cuello 2006; Carilla et al. 2018). *F. punensis,* in Argentina, is located in the Provinces of Catamarca, Jujuy, La Rioja, Salta, San Juan and Tucumán, between 2200 and 3700 m.a.s.l. *F. bryoides* grows in Jujuy, Salta and Catamarca between 3200–4900 m.a.s.l.; *F. densa* in Jujuy, Salta, Catamarca and Tucumán between 2800–4300 m.a.s.l.; and *F. patagonica* in Jujuy, Salta, Tucumán, Catamarca, La Rioja, San Juan, Mendoza, San Luis, Río Negro, Neuquén, Chubut

and Santa Cruz, between 1200–4000 m.a.s.l. At present, there is no major concern about the cultivation and domestication of species of this *Fabiana* species from Argentina (Barboza and Hunziker 1993, 1998).

7 Ecological Requirements

The native populations of these four *Fabiana* species grow on arid regions, poor quality soils, with limited water supply (Cuello et al. 2011; Carilla et al. 2018). The four *Fabiana* species discussed in this chapter grow in Argentina, Puna, Pre-Puna and Monte. regions characterized by their aridity. The *Fabiana* species are generally found in sandy, rocky soils, with very low fertility values, little organic matter and variable salt content. The flowering of these species occurs in summer and they bear fruit in summer-autumn. In very cold and high climates, flowering occurs early, from October to December in this Hemisphere, while in hot climates, flowering lasts until early Autumn (Alaria and Peralta 2013).

8 Traditional Use (Part(s) Used) and Common Knowledge

These species have been employed as medicines, building material, forage, fuel and elements in spiritual activities (Villagrán and Castro 2000; Villagrán et al. 2003; Rodríguez 2004, 2005; Pérez 2006; Barbarán 2008). Resinous exudate from leaves of *Fabiana* species is used in traditional medicine to immobilize fractured extremities (De Lucca and Zalles 1992; Erazo et al. 2002; Pérez 2006) while the infusion for cough and illness of the lungs (Munizaga 1988), as vulnerary and anti-inflammatory (Pérez 2006). There is archaeological evidence of the use of the woody stems of these species in incenses (Rodríguez 2013a, 2013b; García et al. 2018). Particularly its use as incense stick, where its bioactive compounds can be volatilized and efficiently incorporated into the body through smoke inhalation and cause effects on the health of living beings. In this sense, along with the boiled, crushed, roasted, baths or infusions, scrubs or plasters, are also the smokehouses (Aldunate et al. 1981; Fernández 1995; Villagrán and Castro 2004).

9 Modern Medicine Based on Its Traditional Medicine Uses

Several reports demonstrate the potential health benefits and the scientifically validated of popular medicinal uses of *Fabiana* species.

Antioxidant and Anti-inflammatory Activities Lipoxygenase plays a key role in the biosynthesis of leukotrienes, pro-inflammatory mediators. Hyaluronidase is

determinant in chronic inflammations and allergic processes in humans. Thus, lipoxygenase and hyaluronidase inhibitors initially attracted attention as potential agents for the treatment of inflammatory and allergic diseases, but their therapeutic potential has been expanded to certain types of cancer and cardiovascular diseases. Most lipoxygenase and hyaluronidase inhibitors are also antioxidants or free radical scavengers (Torres-Carro et al. 2019). Cuello et al. (2011) have demonstrated inhibitory effects of ethanolic extracts of *F. punensis, F. patagonica*, *F. densa* and *F. bryoides* on lipoxygenase and hyaluronidase activities. The alcoholic extract of *F. punensis* was an active scavenger of DPPH and ABTS radicals as well as *F. densa, F. patagonica* and *F. bryoides* extracts (Cuello et al. 2011; Isla et al. 2018). *Fabiana patagonica* extracts exhibited the highest peroxyl radical scavenging activity compared with the other three taxa (Cuello et al. 2011). Antioxidant activity of *F. densa* tea and *F. punensis* essential oil was also demonstrated (Rojo et al. 2009; Rodríguez et al. 2018).

Antibacterial Activity The phenolic compounds enriched ethanolic extracts of *F. bryoides, F. densa, F. punensis* and *F. patagonica* inhibited the growth of one or more of the commercial antibiotic resistant human pathogenic strains*: Staphylococcus aureus, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Enterobacter cloacae, Morganella morganii, Pseudomonas aeruginosa* (Zampini et al. 2009; Isla et al. 2018). The ethanolic extracts exhibited stronger activity and broader spectrum of action than aqueous extracts. The extracts were bactericidal in most cases and more active on Gram (+) than Gram (−) bacteria (Zampini et al. 2009). Antibacterial activity of two diterpenes isolated (the succinoyl and the oxaloyl esters of the *ent*-beyer-15-en-18-ol) from *F. densa* exudates against Gram (+) and Gram (−) bacteria were also demonstrated (Erazo et al. 2002). Recently, a key role played by the acidic group at C18 of the tetracyclic *ent*-beyerene for the antibacterial effects was described. It was also highlighted how the length and flexibility of the alkyl chain between the two carbonyl groups are crucial factors for the biological activity of the molecule (Quaglio et al. 2020). These finding support the usage of these species for the development of new anti-infective drugs.

Diuretic Activity A moderated diuretic activity of *F. patagonica* extract was reported by Álvarez et al. (2002) and it was suggested to be associated with the presence of oleanolic acid, which was isolated as the major metabolite in *F. patagonica* infusion.

According to above mentioned, these *Fabiana* species have a potential to serve as a raw material for medicinal products. Based in our review, *F. punensis*, *F. bryoides*, *F. densa* and *F. patagonica* are likely candidates as species of economic interest in Argentina (Cantero et al. 2019).

10 Conclusions

The *Fabiana* species herein reviewed (*F. bryoides, F. densa, F. punensis* and *F. patagonica*) that grow in arid regions of Argentina, are popularly used as medicinal plants. The effectiveness of these plants as inhibitors of inflammatory mediator liberation, or as anti-infective and diuretic, described in their traditional use, are supported by recent investigations. As medicinal plants, they could be used to promote the development of new chemical derivatives, as well as products. More chemical studies are needed to standardize their bioactive extracts and to elaborate good practices for their production. Typically, these should include various stages of production, from the harvesting in wild growing populations until the selection of germplasm for cultivation trials.

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