



## Review

## *Arbutus unedo* L.: From traditional medicine to potential uses in modern pharmacotherapy



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## ABSTRACT

**Ethnopharmacological relevance:** *Arbutus unedo* L., the strawberry tree (Ericaceae family) is of increasing interest because of its common traditional, industrial, chemical and pharmaceutical uses. The plant is a typical evergreen plant of the Mediterranean basin, as well as of other regions with hot summers and mild rainy winters. This review covers the studies relevant to *Arbutus unedo* L. utilization in the current pharmacological therapy.

**Materials and methods:** The available information on traditional uses, phytochemistry and biological activities of *Arbutus unedo* L. was collected from scientific databases through a search using the keywords '*Arbutus unedo* L.' and/or 'strawberry tree' in 'Google Scholar', 'Pubmed', 'Scencedirect', 'SpringerLink', 'Web of Science - Clarivate Analytics' and 'Wiley'. Unpublished Ph.D. and M.Sc. dissertations were also consulted for chemical composition, biological activities and traditional uses of *Arbutus unedo* L. and for manual search of additional references.

**Results:** The fruits of the plant have been traditionally used as antiseptics, diuretics and laxatives in folk medicine, while the leaves have been used due to their diuretic, urinary antiseptic, antidiarrheal, astringent, depurative and antihypertensive properties. According to the scientific literature survey, different extracts obtained from *Arbutus unedo* L. have demonstrated a high pharmacological potential due to their *in vitro* and preclinical antibiotic, antifungal, antiparasitic, antiaggregant, antidiabetic, antihypertensive, anti-inflammatory, antitumoral, antioxidant, and spasmolytic properties.

**Conclusion:** This review suggests that *A. unedo* is a promising source of phytopharmaceutical products. The potential advantages of *Arbutus unedo* are related with the presence of polyphenolic compounds in its composition. However, further studies are needed to ascertain some profitable effects in humans. The beneficial effects associated with this shrub suggest that *Arbutus unedo* can be used for the development of new drugs to treat diseases such diabetes, hypertension, among others. Nonetheless, the safety of the *Arbutus unedo* compounds should also be examined.

## 1. Introduction

Many plant species could be used as sources of high value chemicals

(such as bioactive compounds) for their secondary metabolites. *Arbutus unedo* L. (*A. unedo*, Ericaceae family), commonly known as the strawberry tree, is an evergreen shrub or small tree, normally between 1.5 m

**Abbreviations:** AAPH, 2,20-azobis(2-amidinopropane) dihydrochloride; ABTS, 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid); A. unedo, *Arbutus unedo* L.; BrdU, 5-bromo-2'-deoxyuridine; COX-2, Cyclooxygenase-2; DPPH, 2,2-diphenyl-1-picrylhydrazyl; FRAP, Ferric ion reducing antioxidant power; GAE, Gallic acid equivalent; IL, Interleukin; IVGTT, Intravenous glucose tolerance test; L-NAME, N<sup>G</sup>-nitro-L-arginine methyl-ester; MIC, Minimal inhibitory concentration; MMP, Matrix metalloproteinase; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; NO, Nitric oxide; NOS, Nitric oxide synthase; OGTT, Oral glucose tolerance test; ORAC, Oxygen radical absorbance capacity; PUFA, Polyunsaturated fatty acids; ROS, Reactive oxygen species; SRB-, Sulforhodamine B; STAT, Signal transducer and activator of transcription; TBARS, Thiobarbituric acid reactive substances; TEAC, Trolox-equivalent antioxidant capacity; TNF, Tumor necrosis factor

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Fig. 1. *Arbutus unedo* tree (A); Ripe (B) and unripe fruits (C); *Arbutus unedo* flowers (D). Adapted from (Oliveira, 2010).

and 3 m tall (Fig. 1), native to the Mediterranean region, but also found in other regions characterized by hot summers and mild rainy winters (Fig. 2) (Celikel et al., 2008; Molina et al., 2016; Torres et al., 2002).

The trees show high resistance to hard environmental conditions like drought, low temperatures and heavy or poor soil conditions (Gomes and Canhoto, 2009). They also show rapid regeneration after forest fires (Arnan et al., 2013). The *A. unedo* tree's high resistance to harsh environmental conditions is particularly important with regard to fauna diversity and soil erosion prevention. From the ecological point of view, the resistance of *A. unedo* plays a pivotal role in forestation programs in southern European countries such as Greece, Italy, Portugal and Spain, where fires are common during the dry season (Schröter et al., 2005).

The ornamental, nutritional and medicinal value of *A. unedo* has been recognized since Greek times (Ruiz-Rodríguez et al., 2011). The production of red fruits and pinkish-white flowers, which appear during the winter, increase its crop value and ornamental uses (Males et al.,

2006).

The fleshy edible fruit of *A. unedo* has been a part of the Mediterranean diet (Molina et al., 2011; Ortuño Moya, 2003; Ruiz-Rodríguez et al., 2011; Tardío et al., 2016). This fruit is usually consumed as jam or marmalade, or distilled into liquor (Rivera et al., 2006; Soufleros et al., 2005; Tardío et al., 2006). *A. unedo* fruits are a source of health, namely of vitamin C and dietary fibers, while also rated as a source of bioactive compounds for dietary supplements or functional foods (Ruiz-Rodríguez et al., 2011). This plant is traditionally referred as melliferous (Guzman Tirado, 1997) and strawberry-tree honey is very appreciated for its characteristic bitter taste and presumed biological properties, besides its remarkable economic importance (Tuberoso et al., 2013, 2010). *A. unedo* stems and leaves are used for hardening olives (Tardío et al., 2006).

Nonetheless, this plant remains largely underexploited and organizations such as Food and Agriculture Organization (FAO) are currently undertaking to increase the use of this species (FAO, 2010).

The different parts of this plant and strawberry-tree honey have been used in folk medicine to treat a large number of diseases (Kivçak and Mert, 2001; Morales et al., 2014; Spano et al., 2009; Tuberoso et al., 2010; Verde et al., 1998; Ziyat et al., 2002).

*A. unedo* is generally regarded as a wild edible plant, but the significance and potential use for both medicinal and non-medicinal purposes, have led to the development of several ethnobotanical studies aiming to describe traditional uses, particularly in Iberian Peninsula (Carrió and Vallès, 2012; González et al., 2010; Guzman Tirado, 1997; Menendez-Baceta et al., 2012; Ocaña, 2000; Verde et al., 2006). Thus, besides the above mentioned uses as food or for liquors preparation, this plant is also described for animal feeding (Guzman Tirado, 1997; Ocaña, 2000). These ethnobotanical studies have demonstrated the ethnopharmacological importance of this species and several descriptions on the use of different parts of this plant in folk medicine, mainly in decoctions or infusions, are presented in Table 1.

The described medicinal characteristics are related to the contents of several pharmacotherapeutically active compounds in different parts of *A. unedo*. The plant contains a wide variety of antioxidant compounds (carotenoids, organic acids, phenolics, terpenoids, vitamins E and C) as well as compounds with antimicrobial, antiaggregant, anti-diabetic, antihypertensive, anti-inflammatory and antitumoral properties (Carcache-Blanco et al., 2006; Tavares et al., 2010). The rationality of *A. unedo* uses in traditional medicine has been demonstrated by some reports, which will be discussed in later sections of this review. The phytochemical content of the different parts of the *A. unedo* tree (leaves, fruits, bark, wood/stalks and roots) have been the subject of several studies (Delgado-Pelayo et al., 2016; Erkekoglou et al., 2017; Fonseca

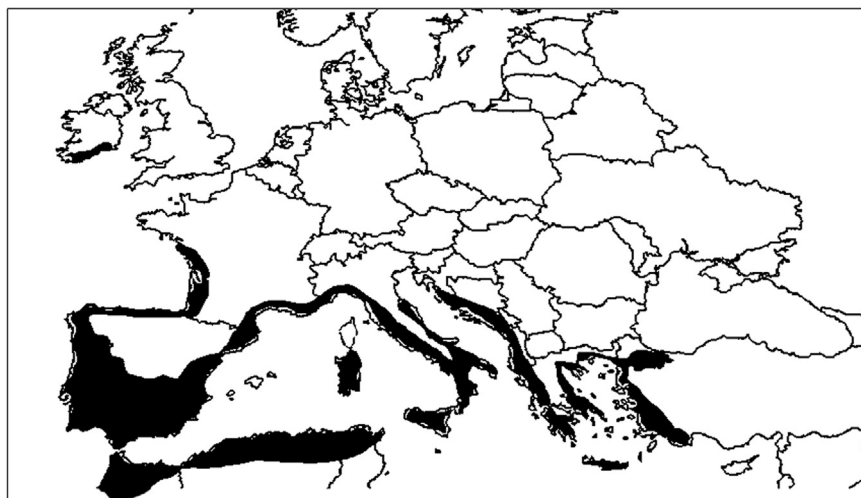


Fig. 2. Worldwide distribution of *A. unedo*. Adapted from (Oliveira, 2010).

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