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Review

The génépi *Artemisia* species. Ethnopharmacology, cultivation, phytochemistry, and bioactivity

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ABSTRACT

Wormwoods (*Artemisia* species) from the génépi group are, along with Edelweiss, iconic plants of the Alpine region and true symbols of inaccessibility because of their rarity and their habitat, largely limited to moraines of glaciers and rock crevices. Infusions and liqueurs prepared from génépis have always enjoyed a panacea status in folk medicine, especially as thermogenic agents and remedies for fatigue, dyspepsia, and airway infections. In the wake of the successful cultivation of white génépi (*Artemisia umbelliformis* Lam.) and the expansion of its supply chain, modern studies have evidenced the occurrence of unique constituents, whose chemistry, biological profile, and sensory properties are reviewed along with the ethnopharmacology, botany, cultivation and conservation strategies of their plant sources.

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1. Introduction

Infusions of plants in alcohol are popular in both European and Asian countries, as exemplified by medicinal wines, mulled wines, and medicinal sakes like the Japanese Toso [1]. In this context, plants from the genus *Artemisia* have long been used to flavour alcoholic beverages, giving them a bitter taste and alleged tonic properties. Historically, the Roman *vinum absinthiatum* can be considered an early precursor of what is known today as vermouth [2], and the growing popularity of absinthe, now legal in Europe if complying with the regulatory limits for thujones in alcohol beverages (35 mg/L) [3], further testifies the interest of consumers for this type of beverages. The literature on plant-enriched alcoholic beverages is dominated by studies on absinthe wormwood (*A. absinthium* L.), and little systematic attention has so far been dedicated to the Alpine *Artemisia* species that are used for the production of the celebrated liqueur génépi [4]. One major reason is, undoubtedly, the very limited availability of these iconic plants of the Alpine landscape, since collection in the wild is, depending on the location, either forbidden or severely limited, and domestication has been achieved only recently. Cultivation has been at the basis of the recent growing popularity of génépi-based products (liqueurs, teas, syrups, candies, chocolates, cakes, jams, mustards), a trend that, in turn, has fostered studies aimed at the isolation of compounds useful as markers to fight adulteration. The literature on génépi is scattered and no review article has been published on this topic so far, providing a rationale for summarizing current knowledge on the botany, cultivation and phytochemistry of the Alpine wormwoods from the génépi group, as well as on the molecular- and sensory pharmacology of their constituents.

2. Ethnopharmacology

Limited systematic work has been done so far on the ethnopharmacology of the alpine region of Europe [5]. Local knowledge on medicinal and food plants has mainly been transmitted through oral tradition, and might therefore be in part lost due to the sharp decrease of population observed in the past century and the dramatic changes in lifestyle related to the demise of agriculture and other traditional activities of the alpine economy [5]. In this context, génépi is an exception, since its medicinal properties have been documented at least from the second half of the XVIII century. Thus, unlike absinthe, that was, and growingly is, essentially consumed as a recreational beverage, génépi and its source plants have always been associated with medicinal properties. This was vividly testified by the philosopher Jean Jacques Rousseau who, in a famous passage of his *Confessions*, described the death of the gardener Claude Anet, who had gone on an Alpine trip to collect génépi for a physician (Monsieur Grossi) [6]. Possibly because of the weather and the fatigue associated with reaching the habitat of the plant, the gardener, who should be credited for the life-long interest of Rousseau in plants and botany [7], came back with pleurisy. The condition could not be treated with génépi, considered at that time one of the remedies of choice for pleurisy, and the gardener eventually succumbed to the disease [*…ce pauvre garçon s'échauffa tellement, qu'il gagna une pleurésie, dont le Génipi ne put le sauver, quoiqu'il y soit, dit-on, spécifique* (a pleurisy that genipi could not relieve, though said to be specific in that disorder)] [8].

In folk medicine, génépis are used as thermogenic agents to fight cold, a use testified by the credence that when sheep eat these bitter plants, the night will be very cold [9]. The association of génépi with cold resistance might be related to the thick hairy layer that covers the plant, a protection against the low temperatures of its environment (as well as against the sun). Infusions of génépis are used to fight cold and fever and stimulate perspiration, while wines aromatized with these plants are believed to stimulate appetite, promote digestion, and fight mountain sickness [4]. Like other asteraceous plants, génépis are used topically as wound-healing agents and to resolve bruises, like in the "Vulnéraire Suisse" or "Falktranck" that was celebrated in the ancient European pharmacopoeias [4].

Bitter liqueurs became popular as tonic medicines in the XIX century, and remained so until the first half of the past century. During the prohibition time, Fernet Branca remained, in fact, the only spirit legally sold in US, to the point that an American distillery for its production was opened in New York City's Tribeca [10]. Because of the rarity of the plant and the difficulty of its collection, the large-scale industrial production of the liqueur génépi started relatively late compared to absinthe and other liqueurs, being first documented only in 1827–1840 at Maison Chavasse near Chambéry in Savoy, at that time part of the Kingdom of Piedmont [11]. During the second half of the XIX century, génépi enjoyed a stellar fame for its digestive properties, immortalized by the comment of De Amicis, the author of the children book *Heart* (*Cuore*), who enthusiastically defined it "un liquore di fiori di prato che farebbe digerire una bomba lessa" (a liqueur of field flowers that would make you digest a boiled bomb) [12]. The consumption of the liqueur declined with the ban of absinthe in the early XX century, but increased with the popularity of winter sports since the 1970s, with génépi becoming a popular après-ski drink. However, its consumption has so far been substantially limited to the Alpine environment, although it can be found in premium liqueur stores in all major European cities. Because of the thujone regulation, the commercialization of génépi in the USA is limited to products that are prepared from thujone-free chemotypes of the plants [3]. Over the past decade, the production of the liqueur génépi has started also in central Italy, since one of the alpine génépi species (*Artemisia eriantha* Ten.) also grows in the high regions of the Appenines, and cultivation experiments have been successfully carried out in the Abruzzo region of Central Italy [13]. Although there are many commercial producers of génépi, it is difficult to provide an estimation of the overall harvest of the plant, since home production is widespread in the Western Alpine regions. The traditional recipe follows the so called *rule-of-four*, meaning that each litre of 40% alcohol requires 40 g of sugar and 40 flower heads [4].

3. Botany, genetics and conservation

3.1. Botany

The etymology of the name génépi is controversial. It might derive from the Arpitan dialect *zhènépi* or *jnépi*, a name used for several *Artemisia* species in Savoy (France), but a derivation from the Latin *Dianae spicum*, meaning 'Diana's ear' in reference to the shape of the inflorescence, has also been proposed [14]. In the Alps, the name génépi is used to refer to five perennial and aromatic *Artemisia* species (Table 1), traditionally collected from wild populations to produce digestive liquors and herbal teas.

Artemisia umbelliformis Lam., also called Alpine wormwood or white génépi, is the most widespread and easy to cultivate. *A. genipi* Weber, the so called black génépi, is the favourite species of liquor producers. *A. eriantha* Ten. is not often used for génépi, growing mainly in the Mediterranean Alps and in the Apennines. *Artemisia glacialis* L. is the least aromatic species and is rarely used to produce génépi. Even more rarely