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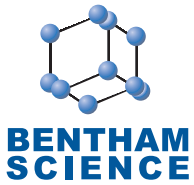
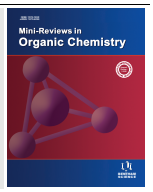
REVIEW ARTICLE



Review: *S*econdary Metabolites of *Aquilaria*, a Thymelaeaceae Genus



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ARTICLE HISTORY

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Abstract: ***Background:*** Aquilaria, a genus belonging to the Thymelaeaceae, produces fragrant resinous agarwood, also known as eaglewood, which has been used as incense since old times. The intense fragrance is the result of the presence of a wide variety of secondary metabolites.

Objective: This genus was reported contained sesquiterpenes, chromones, flavonoids, benzophenones, diterpenoids, triterpenoids, and lignans.

Conclusion: Here, we review the different secondary metabolites that have been identified in Aquilaria to show their diversity and to allow comparison with other Thymelaeaceae genera.

Keywords: *Aquilaria*, Thymelaeaceae, sesquiterpene, chromone, flavonoid, benzophenone, diterpenoid, triterpenoid, lignan.

1. INTRODUCTION

The Thymelaeaceae are a family of dicotyledonous plants mainly found in the tropics and subtropics. They are mostly trees and shrubs, but include also a few vines and herbaceous plants. The family is especially diverse in the southern hemisphere, with many different species present in Africa and Australia [1]. Some species can also be found in Europe, and in parts of Asia and South America, but, in these latter regions, their diversity is much less [2]. Some genera are commercially grown for their sweet-scented and fragrant flowers. Other genera are cultivated for their hardwood, for their bark, which is a raw material for paper making, or for their odorous, highly resinous wood (agarwood), which is used for incense and perfume production.

Thymelaeaceae synthesize many, highly diverse secondary metabolites with a wide range of bioactivities, which has led to numerous applications of Thymelaeceae plant extracts in traditional medicine. For instance, in Kampo medicine in Japan, agarwood preparations are used as sedative, analgesic or digestive [3]. In China, *Aquilaria* leaves are applied topically to treat injuries such as fractures and bruises [4], and, in Korea, agarwood has been used for the treatment of cough, asthma, and as a sedative among others [5].

A completely different application exploits the strong fragrance of Thymeleaeceae plants, in particular of *Aquilaria* species. In Saudi Arabia and other Arabic countries, the wood of *Aquilaria* trees is used as incense at important religious occasions [5, 6]. Wood from closely related species is used during Budhist ceremonies in Asian countries such as Japan and India. Interestingly, the fragrant agarwood resin is not produced in normal wood tissues, but it is only formed when the plant is injured, *e.g.,* by wind, lighting, gnawing by ants or insects, or by microbial infection. These natural processes are slow and occur by chance, causing the agarwood to develop very slowly over decades. Therefore, agarwood is also produced artificially by burning, holing, cutting, or deliberate inoculation of the trees with fungi such as *Fusarium* spp [7-10]. Nevertheless, despite the artificial production, the demand for agarwood far exceeds the available supply, fostering a deep interest in the secondary metabolites that are responsible for the fragrance properties of agarwood

Widely studied *Aquilaria* species include *A. sinensis, A. malaccensis, A. crassna*, and *A. agallocha.* Depending on the region where these species grow, different names are used for the produced agarwood, such as Eaglewood, Gaharu, Kanankoh, Jinkoh, Chen Xiang or Tram [8, 9]. It is also called aloeswood or agalloch [8]. Each species produces agarwood with different fragrance properties, depending on the variety and quantity of the secondary metabolite content, especially sesquiterpenes and chromones. To assist in the search for alternative sources of agarwood-like fragrant resins, we review here the different secondary metabolites that have so far been characterized in *Aquilaria*.

There are two reviews that have been published that discussed about the same genus [11, 12]. These previous reviews did not discuss several classes of compounds such as diterpenoid, benzophenon, lignan and used references before 2011. Otherwise, this review was compiled using references, mostly published in 2001-2016. Some references which were dated before 2000 showed that the study of this genus had lasted for longtime. Another review published in 2016 discussed more on bioactivity of compounds contained in this genus [13].

2. PHYTOCHEMISTRY ASPECTS

2.1. Sesquiterpenes

The fragrant sesquiterpenes that have been found in the *Aquilaria* genus include compounds with a guaiane, eudesmane/selinane, eremophilane/nootkatane, agarofuran, vetispirane/agarospirane, or prezizane skeleton (Fig. **1**). Most of these sesquiterpenes are oxygenated [14-16].

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