

Review Article

Phytochemistry and medicinal values of *Mahonia bealei*: A review

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Abstract

Purpose: To review the medicinal uses of *Mahonia bealei*, an important member of the genus *Mahonia*, with a focus on its various applications in Traditional Chinese Medicine, as well as published scientific evidence on its effectiveness.

Methods: Information in all available literature was retrieved using different search engines including NCBI, ISI Web of Knowledge and Google.

Results: Several compounds have been extracted from *M. bealei*. These include alkaloids, triterpenes, flavonoids, phytosterols and lignans. Traditionally, the plant is used to treat dysentery, diarrhea and inflammation. Globally, scientists have used *in vitro* and *in vivo* techniques to evaluate the usefulness of compounds extracted from *M. bealei* with respect to their antibacterial, anti-inflammatory, antitumor, antioxidant as well as anti-gastrin properties.

Conclusion: Different parts of this plant still remain underexplored. Moreover, comparison of the properties of the isolated compounds has not been carried out, nor are there reports on the synergistic effects of extracts of the plant. Therefore, future research to address these areas may be useful in the discovery of new therapeutic agents.

Keywords: Berberidaceae, *Mahonia bealei*, Traditional Chinese Medicine, Alkaloids, Flavonoids, Anti-inflammatory activity, Anti-tumor activity

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INTRODUCTION

Mahonia bealei belongs to the family Berberidaceae and genus *Mahonia*. Geographically, this evergreen shrub is widely distributed in America, Europe and Asia [1]. *Mahonia* is a genus containing more than 60 species, and more than 30 species of this genus

grow in the southwest area of China [2]. The genus *Mahonia* is a member of basal eudicots which consists of coriaceous (sclerophyllous) evergreen small trees or shrubs with compound leaves [2,4]. It has been revealed that 20 species of this genus are distributed in southwestern parts of the United States of America [4]. Some of the species are also present in Europe as

invasive plants [5].

Traditional Chinese Medicine (TCM) has a long history of usage of materials derived from botanical, animal as well as mineral resources. These agents have been classified according to their sources, color, habitats, way of collection, parts of the plant collected and the methods of prescription, by Li in his famous work *Ben Cao Kong Mu* (The Classical TCM Pharmacopeia) [6]. In TCM, the roots, stem and leaves of *Mahonia* have been used for the treatment of different diseases such as diarrhea and dysentery for centuries. These plants are recognized by the Chinese Pharmacopeia Commission for their moisturizing effects, *heat-clearing* properties, and as detoxifying agents [7].

Another important species with similar properties reported in TCM is *bai-yang-jie* (*Arundina graminifolia*) [8]. In TCM, *Mahonia Caulis* which comprises dried stem of *Mahonia bealei* (Fort.) Carr. and *M. fortune* (Lindl.) Fedde is an important medicine. It has been used for long for treating icteric hepatitis, conjunctivitis, ulcers, boils, carbuncles, toothache, and ailments that were thought to be due to *fire of stomach* [9]. The leaves of *Mahonia bealei* have been used to produce bitter tea, and are rich in polyphenolic compounds with potent antioxidant properties [10]. There have been numerous reports showing the antioxidant potential of the leaves when consumed in the form of tea like black tea which is used worldwide [11].

Studies have shown that the chemical composition of different compounds from *Mahonia bealei* is important for their use in pharmaceutical industry [1,12,13]. The leaves of *Mahonia bealei* are an important source of beneficial natural compounds that need to be explored [14]. Phytochemical studies have revealed that the stem and roots of *M. bealei* are rich in cerebrosides and alkaloids [15]. Different parts of the genus *Mahonia*, such as stem, bark, leaves and fruits of have been extensively used, and possess a long history of application in TCM [16-20]. Phytochemical studies on *Mahonia* species have been very beneficial in the isolation of sterols, alkaloids, flavonoids and glycosides [1].

The present study summarized the number of useful compounds isolated from *Mahonia bealei* and their structures. In addition, the medicinal uses of these compounds were reviewed, and a comparison of the medicinal uses of the plant in TCM, in relation to experimental findings was made. Future prospects regarding studies of this species were also proposed in this review.

Morphology and distribution of *Mahonia bealei*

Mahonia bealei (also called leatherleaf *Mahonia*) is an evergreen shrub that grows to a height of about 5 to 10 feet (1.5 to 3 m). Pinnately compound leaves are present which are 18 inches (46 cm) long and contain 9 - 13 holly-like leaflets 1 to 2 inches (2.5 to 5.1 cm) wide, and 2 to 4 inches (5 to 10 cm) long. The time of flowering of this plant is from late winter to early spring. The flowering starts with the development of fragrant, lemon-yellow flowers. The fruits are green berries which later turn to blue black color and increase in size to half an inch, while hanging from the plant. Although the plant is native to China, it is an invasive plant in parts the United States of America, especially the southern region, and it has been categorized as an ornamental shrub [21]. Figure 1 shows the different parts of this plant.



Figure 1: *Mahonia bealei*. (a): The aerial parts of *Mahonia bealei* growing among other plants; (b): leaves of *M. bealei*; (c): roots of *Mahonia bealei*; (d): fruits of *Mahonia bealei*

Compounds isolated from *Mahonia bealei*

The extraction of compounds from medicinally important plants and investigations of their medicinal uses are important areas of scientific research. Different parts of *Mahonia bealei* have been studied. In this section, the number, nature and structure of compounds isolated from this species to date, are summarized.

Alkaloids

Studies have shown that isoquinoline alkaloids constitute a major subclass of alkaloids isolated from the genus *Mahonia*. These compounds are responsible for many properties exhibited by plants of this genus. A study has shown that the roots, stem and leaves of *M. bealei* contain the three alkaloids berberine, palmatine, and jatrorrhizine [22]. The major alkaloid found in leaves was berberine, while the roots and stem contained jatrorrhizine and berberine [23]. The structures of these alkaloids are given in Figure 2 and Figure 3 [30].

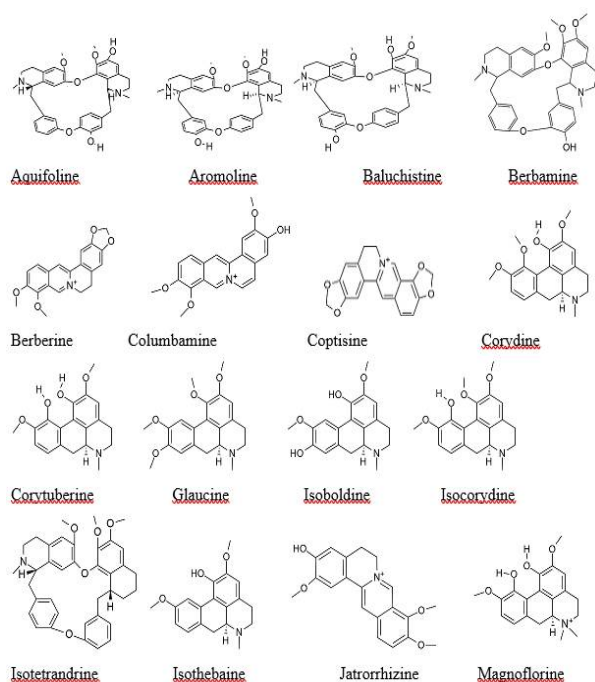


Figure 2: Structures of alkaloids isolated from *Mahonia bealei*

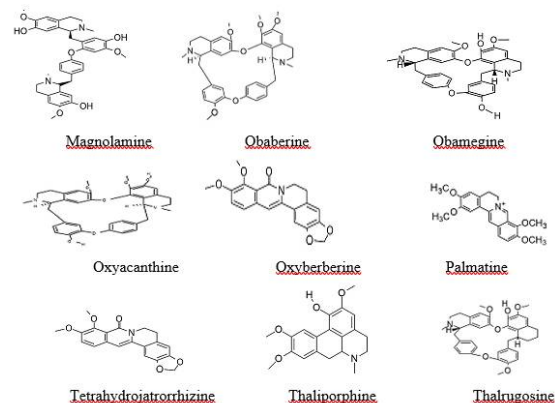


Figure 3: Structures of alkaloids isolated from *Mahonia bealei*

Triterpenes

To the best of our knowledge, so far, only three triterpenes have been isolated from the leaves of *M. bealei*. These compounds, identified as ursolic acid, oleanolic acid and oleanolic acid 3-O- β -D-glucopyranoside, were for the first time isolated from the species of the genus *Mahonia* [15]. Later-on, 3-O- β -D-glucopyranoside was isolated from the branches of this plant [24]. The structures of these triterpenes are given in Figure 4.

Flavonoids

Certain flavonoids have been isolated from the leaves and branches of *M. bealei*. These

flavonoids are quercetin and quercetin 3-O- β -D-xylopyranoside [25]. Later studies also reported the isolation of tamarixetin 3-O- β -D-glucopyranoside, quercetin 3-O- β -D-xylopyranoside, isorhamnetin 3-O- α -L-rhamnopyranoside, luteolin, isorhamnetin, tricetin, and chryseriol. The structures of these flavonoids are shown in Figure 5.

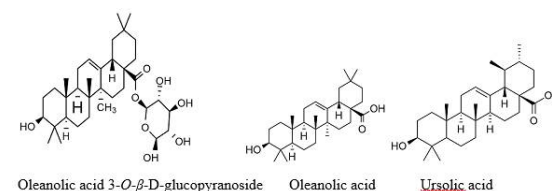


Figure 4: Structures of triterpenes isolated from *M. bealei*

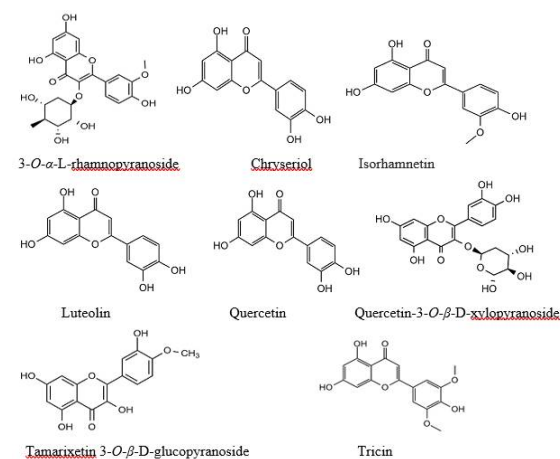


Figure 5: Flavonoids from *M. bealei*

Phytosterols

Two phytosterols have been isolated from *Mahonia bealei*. A stigmasterol was reported after NMR and MS spectroscopic studies of methanol extract of the plant [25]. In another study, 70 % ethanol extract of the stem of *Mahonia bealei* yielded β -sitosterol [26]. The structures of these phytosterols are shown in Figure 6.

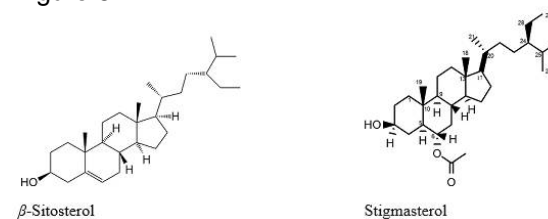


Figure 6: Phytosterols isolated from *M. bealei*

Lignans

Four lignans have been isolated from *Mahonia bealei*. A study of 70 % ethanol extract of the

stem of *Mahonia bealei* using chromatographic separation techniques yielded episingaresinol which was characterized by mass spectrometry [26]. Later on, another study conducted on the ethyl acetate fraction of the trunk of *M. bealei* yielded three more lignans identified as yangambin, epiyangambin and bishexadecyl epiphyllate [25]. The structures of these lignans are given in Figure 7.

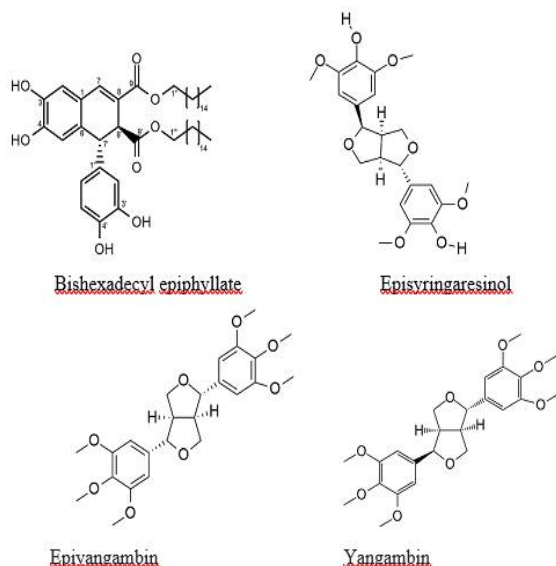


Figure 7: Lignans isolated from *M. bealei*

Other compounds isolated from *M. bealei*

In addition to the classes of compounds already presented, several compounds from other classes have been isolated, although in less abundant amounts, from different parts of *M. bealei*. Erythro-syringoyl glycerol 8-O- β -D-glucoside; 3, 4, 5-trimethoxyphenyl-1-O- β -D-glucoside, and 5,5'-dimethoxylariciresinol- 4'-O- β -D-glucoside were identified from the stem extracts of *M. bealei* [26]. Another study isolated three compounds belonging to phenolic, steroidal and phenylpropanoid groups. These were identified as methyl syringate, daucosterol, and 3-(4-hydroxy-3, 5- dimethoxyphenyl)-3-ethoxy-2-sulfopropane-1-ol, respectively. Later on, gallic acid and trans-cinnamic acid were identified from extracts of the branches of *Mahonia bealei* after isolation, purification and characterization [24]. The structures of these compounds are given in Figure 8.

MEDICINAL USES OF COMPOUNDS ISOLATED FROM *M. BEALEI*

Several medicinal uses of the compounds extracted from *M. bealei* have been reported. These are reviewed below.

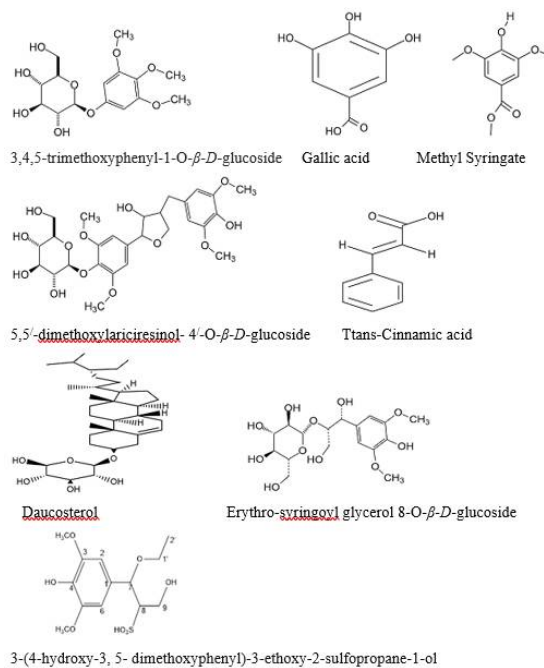


Figure 8: Other groups of compounds isolated from *M. bealei*

Antimicrobial properties

In TCM, the plants from genus *Mahonia* are known to inhibit bacteria. *Mahonia caulis* consists of *M. bealei* (Fort). Carr and *M. fortune* (Lind.) Fedde. These plants were used as anti-pneumoconiosis, anti-nociceptive, as well as antipyretic agents [27,28]. Studies have shown that ethanol extracts of stems and leaves of *M. bealei* are effective against *Staphylococcus aureus*, *Bacillus thuringiensis* and *Bacillus subtilis*, but not effective against gram positive bacteria. The stem extract of *M. bealei* was more effective than the leaf extract. The most effective antimicrobial activity exhibited by the stem extract was against *Staphylococcus aureus*, with minimum inhibitory concentration (MIC) of 0.58 mg/ml, relative to the leaf extract with MIC of 2.30 mg/ml [18].

Another study showed that extracts of *Mahonia bealei*, whether tanninized or de-tanninized, did not show any activity against clinically important multidrug resistant pathogenic strains of *Acinetobacter baumannii* 31P, 125 and 152P [29]. However, a US patent document showed a preparation method for the extract of *Mahonia bealei* that exerted biostatic effects on *Escherichia coli*, *Staphylococcus aureus* and *Enterococcus faecalis*. Inhibitory effect was not reported on *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Enterobacter cloacae*. An important feature of this invention is the simple method of extract preparation using the stem and

leaves of *Mahonia bealei* as raw materials, with water, ethanol or water-containing alcohol as solvent. This patent emphasizes the antibacterial activity of *M. bealei* [30]. It has been reported that alkaloid extract of the roots of *M. bealei* (Fort.) Carr. inhibited the proliferation of Avian influenza virus (AI) in embryos at a dose of 0.25mg/ml, and showed no adverse side effects on the experimental embryos, even at doses up to 20 mg/ml [31].

Antitumor properties

A study has reported that water extract of leaves of *M. bealei* inhibited the proliferation of human colon cancer (HT-29) cells [10]. Molecular and chromatographic evidence indicated that the proportion of apoptotic cells increased while the expression of survivin gene was downregulated [10]. The survivin gene is an important member of an apoptotic family of inhibitors which presence results in the prevention of apoptotic cell death while it promotes proliferation of cells. Studies have revealed that survivin gene expression is upregulated in tumors, while its expression is normally downregulated in normal cells [32]. After evaluation of antitumor property in [10], the compound responsible for the antitumor effect was identified through sequential partitioning of the aqueous extract of *M. bealei* leaves using ethyl acetate, *n*-butanol and dichloromethane. Cytotoxicity of each fraction was assessed against HT-29 cells and it was revealed that the dichloromethane fraction was active against HT-29 cell lines. Further studies showed that the anticancer effect was due to the presence of berberine, which had IC₅₀ of 36.54 μM for HT-29 cells [10]. In another investigation, palmatine, an alkaloid obtained from *M. bealei* was shown to exhibit anti-proliferative properties as well as cytokine-lowering effects *in vitro* and *in vivo* [33]. Previous research had shown that an important risk factor for tumor development (including colorectal cancer) was chronic inflammation, while inhibition of inflammatory pathway was effective in preventing the development of colon cancer [34, 35]. *In vitro* studies to check levels of production of LPS-induced inflammatory cytokines showed higher cytokine levels in HT-29 cell lines than in SW-480 cell lines, while the administration of palmatine resulted in significant reduction of IL8 cytokine levels in HT-29 cell lines. Results of *in vivo* studies showed that oral administration of palmatine at doses of 10 or 20 mg/kg/day in APC^{min/+} resulted in significant reduction of tumor numbers in colon and small intestine. Therefore, orally-administered palmatine may have significant therapeutic potential for colorectal cancer [33]. Since palmatine obtained from

Mahonia bealei and orally administered *M. bealei* were used in the above study, it was concluded that *M. bealei* possesses antitumor properties [33].

Antioxidant effects

Studies have shown that free radicals are major causes of oxidative damage to biological molecules as a result of which diseases like cancer, coronary heart disease and dementia develop. Free radicals are also considered major factors in the aging process [35]. A study of the water extract of leaves of *Mahonia bealei* (Fort) Carr. showed that it exhibited antioxidant properties. The stable free radical 2, 2-diphenyl-1-picrylhydrazyl (DPPH) is used for the evaluation of reducing substances in biological systems as well as foods [36]. Experimental evidence revealed that leaf extract of *Mahonia bealei* exhibited DPPH free radical scavenging effect in concentration-dependent manner, with a concentration of 100μg/ml producing the highest (73.67 %) scavenging effect [10]. The superoxide radical brings about oxidative damage to cells [37]. The aqueous leaf extract of *M. bealei* scavenged superoxide anions in a concentration-dependent manner, and significantly reduced oxidative modification of proteins [10]. Proteins are one of the major targets of oxidative damage by free radicals [38]. In another study, it was shown that ethanol extract of *M. bealei* exhibited anti-radical effects against DPPH, with IC₅₀ value of 80.0 μg/ml, and against ABTS⁺ with IC₅₀ value of 26.2 μg/ml [39].

Anti-gastrin effect

Gastric ulcer is an important and common pathological condition that causes loss of weight, loss of appetite, vomiting, heartburn and other clinical manifestations [40]. In the clinical treatment of gastric ulcer, the inhibition of gastric acid secretion is very important because gastric acid has been identified as the key pathogenic factor of the disease [41]. Historically, the introduction of H₂ receptor antagonists and proton pump inhibitors that target gastric H⁺/K⁺-ATPase resulted in a major breakthrough with respect to the treatment of gastroesophageal reflux diseases and peptic ulcer [42,43]. Studies show that gastric H⁺/K⁺-ATPase is responsible for the acidification of stomach. It is a proton pump which stimulates gastric acid production. The inhibition of this pump is useful in clinical treatment of reflux disease, peptic ulcer and dyspepsia [42].

Previous studies showed that other medicinal plants in TCM such as *Dregea sinensis* Hemsl.

(Daibaiji) and *Dracaena cochinchinensis* (Lour.) (also called dragon's blood) exerted gastro-protective effects *in vivo* [44,45]. A study has shown that total alkaloids from the stem of *M. bealei*, when applied on experimental rats lowered the content of gastrin by inhibiting H⁺/K⁺-ATPase activity, resulting in reduction of gastric acidity. A 57 % protective effect of total alkaloids from *M. bealei* was observed on pyloric ligation-induced gastric ulcer in rats *in vivo*, relative to 63 % protection by the positive control omeprazole [13].

Anti-inflammatory effects

Inflammation is an important response that is ubiquitously produced as a defense mechanism against pathogens in all organisms. Macrophages are major immune cells that play a key role in the onset of inflammation [46]. The results obtained from *in vivo* and *in vitro* experiments have indicated that the leaves of *M. bealei* (Fort.) Carr. possess anti-inflammatory properties [47]. A key factor in initiating inflammatory response is the production of NO free radical which acts as a major factor that triggers inflammatory responses [48]. Along with *in vitro* study on cell lines, an *in vivo* study was also conducted using lipopolysaccharide-induced acute lung injury (ALI) in the mouse model. This model was used because inflammatory response is triggered in lung injury, and TNF- α and IL-6 are important indicators of early onset of inflammatory response [49].

Using mouse model, it has been revealed that the levels of inflammatory mediators are reduced by treatment with the dichloromethane fraction of leaves of *Mahonia bealei* (Fort). Carr. [47]. A

study showed that a triterpene obtained from the leaves of *Mahonia bealei* reduced the production of cytokines, downregulated MAPK pathway, and inhibited activation of NF-kB [50].

A summary and comparison of traditional medicinal uses of different parts of *M. bealei*, and scientific evidence reported based on research conducted by different scientists are shown in Table 1.

A summary of classes of useful compounds obtained from different parts of *Mahonia bealei*, their traditional medicinal uses, and scientific evidence obtained to date are presented in Figure 9.

CONCLUDING REMARKS

Mahonia bealei has been traditionally used for medicinal purposes throughout the ancient times. With the advancement of scientific research, scientific evidence is being explored to establish the bases for the uses of the plant. Although several compounds from the roots, stem and leaves of *Mahonia bealei* have been extracted and used in different studies, a lot still needs to be done. A comparison of traditional uses of different parts of *Mahonia bealei* with scientific evidence reported to date shows that many uses of the have not yet been scientifically investigated. Therefore, future research require more studies on different parts of this plant. A comparison of the properties of different solvent extracts of different parts of the plant is also required. More importantly, studies of possible synergistic effects of different extracts may lead to discovery of new therapeutic uses of this plant.

Table 1: Summary of traditional uses of *Mahonia bealei* and reported activities

S/no.	Part of plant used	Traditional uses	Reference	Scientific study	Source	Reference
1	Roots, stem and leaves	Diarrhea	Pharmacopeia [7]	No Reported	-	-
2	Roots, stem and leaves	Dysentery	Pharmacopeia [7]	Not Reported	-	-
3	Roots, stem and leaves	Clearing heat	Pharmacopeia [7]	Antiinflammatory Activity	Leaves	[47,49]
4	Leaves and fruit	Detoxification	Chinese Pharmacopoeia [9]	Antioxidant Activity	Leaves	[10,39]
5	Dried stem	Icteric hepatitis conjunctivitis	Pharmacopeia [7]	Not Reported	-	-
6	Dried stem	Ulcers	Pharmacopeia [7]	Anti-gastrin Activity	Stem	[13]
7	Dried stem	Carbuncles	Pharmacopeia [7]	Not Reported	-	-
8	Dried stem	Toothache	Pharmacopeia [7]	Not Reported	-	-
9	Dried stem	Stomach fire	Pharmacopeia [7]	Anti-gastrin Activity	Stem	[13]

10	Roots	Antipyretic	[27, 28]	Antimicrobial Activity	Stem and Leaves	[18,29-31]
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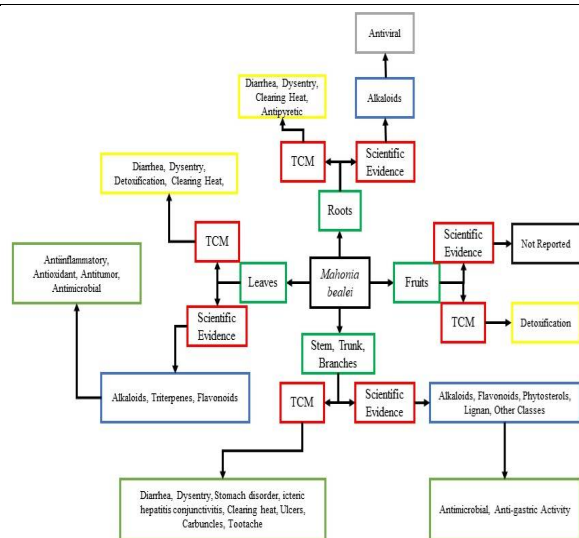


Figure 9: A scheme showing classes of useful compounds obtained from different parts of *Mahonia bealei*, their traditional medicinal uses, and scientific evidence obtained to date

DECLARATIONS

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Mohibullah Kakar generated the idea, searched and compiled the data. Muhammad Saeed and Ke Lou helped in the compilation and searching of data. Imran Suheryani and Wu Shuang helped in the arrangement and writing of the review. Yulin Deng and Rongji Dai provided all the funding and guidelines for the manuscript.

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