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Comprehensive Review of Yemeni *Commiphora myrrha*: Phytochemicals, Extraction Methods, Therapeutic Properties, and Medicinal Applications

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Abstract

Myrrh, derived from *Commiphora myrrha* (C. myrrha) has been valued since biblical times for its use in incense, perfumes, and traditional medicines. Scientific investigations of its chemical composition began more than a century ago. This review compiles recent findings on the historical significance, geographical distribution, traditional medicinal uses, phytochemical constituents, biological activities, pharmaceutical effects, toxicity, and extraction techniques of *C. myrrha*. Particular focus is given to the components of the volatile oil, resin, and gum. Information was sourced from digital databases (PubMed, Google Scholar, Web of Science) and ethnopharmacological literature published between 2000 and December 2024. Traditionally, *C. myrrha* has been used to treat ulcers, pain, digestive and bone disorders, wounds, arthritis, and circulatory problems, particularly in Ayurvedic and Chinese medicines. Pharmacological studies have confirmed its antioxidant, anti-inflammatory, cytotoxic, antimicrobial, hepatoprotective, antiviral, and antiulcer properties, with emerging interest in its potential role in the treatment of Coronavirus Disease 2019. In addition, it is widely used in cosmetics and aromatherapy. Analytical studies have identified essential oils, terpenoids, and steroids, with the resin being particularly rich in bioactive compounds. Future research on the stem, bark, and leaves may uncover additional therapeutic agents.

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1. INTRODUCTION

Over generations and cultures, medicinal plants have played an integral role in human life despite major advancements in pharmaceutical and pharmacological technology [1], [2]. Yemen, with its vast territory and diverse geographical and climatic conditions, is known for its remarkable diversity of plant species distributed throughout the country. Cultivated varieties are estimated to account for approximately 10% of Yemen's approximately 3,000 plant species. These herbs have long been used in traditional Arabic medicine, similar to the Greek and Indian medical systems [3], [4]. According to recent research, fewer than 800 species are still used in the Arab world as traditional medicine to treat many diseases [5]. Plants are the world's largest natural pharmacies, continuously generating abundant bioactive materials [6], [7], such as flavonoids, terpenes, phenolics, and alkaloids [8]. Not less than 25% of drugs are derived from plants in modern pharmacopeia; however, many others are synthetic analogs built on prototype chemical substances isolated from plants [9]. According to one study, 80% of people worldwide use herbal remedies as their primary source of health, because they are inexpensive and safe [3]. Because of the abundance of bioactive chemicals with a variety of pharmacological activities, medicinal plants are well known for their therapeutic uses [10], [11]. Journals, books, theses, reports, and published scientific studies were checked to provide information about *C. myrrha.* The genus *Commiphora*

(Burseraceae), which includes *C. myrrha*, is characterized by its frankincense scent and is one of the richest flowering plant species. It is native to the Arabian Peninsula, subtropical regions of Africa, India, Vietnam, and the western Indian Ocean [12]. They are home to 190 species of trees and shrubs [13], [14]. Some areas of Yemen, such as the southern Hays and southwestern Tihama, are considered areas where myrrh is widespread. Yemen's flora includes eight species of the genus *Commiphora* [12]. Kommis' and 'phora,' a generic epithet, comes from Greek, meaning gum bearer [1], [14]. Myrrh is probably the most famous resin produced by *C. myrrha* (Nees) Engl. is the most widely known species in the genus *Commiphora* [15]. Many small, thorny trees in the genus *Commiphora* (family Burseraceae) produce an aromatic resin, commonly known as myrrh [16], [17]. *C. myrrha* (syn. *Commiphora molmol*) produces myrrh [18], [19]. Different *Commiphora* species have provided products for several applications, including timber, building materials, and natural fencing. However, among aromatic resins, *C. myrrha* holds a distinguished and highly valued position in many species within the genus [20]. Currently, the main source of myrrh is *C. myrrha* [21], which is economically important and yields real myrrh, a resinous exudate (Fig.1).

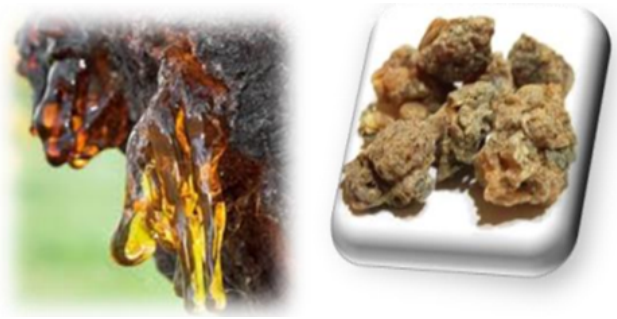


Figure 1. Resinous exudate from *C. myrrha* [22].

The resinous secretion produced by the myrrh tree (Nees Engl) is referred to as the true myrrh [16], [23]. The Arabic word "Murr" translates to "Bitter, "Mir'rah" (Arabic, المر), reflecting both the taste and balsamic aroma of myrrh [24], [25]. Myrrh is known as Mursafi [26], and it has many names around the world, "Hira'bol" (Hindi, हिराबोल) in the Indian subcontinent, "Mò'yào" (Simplified Chinese) in China [19], [27], and "gafal" resin in Sudan [1]. Arabian myrrh is sometimes marketed under the trade name Meetiga and is traditionally called Morr-e-Makki or myrrh [28], [29]. The resin from *C. myrrha* (Burseraceae family) is brittle and breaks along granular fractures. Moreover, it contains thickened, bitter-tasting, or reddish-brown gum. Whenever the bark of a tree splits naturally or is injured, it exudes. When ole gum resin is exposed to air, it hardens into a reddish-brown irregular piece called a 'tear,' which is harvested [30], [31], [32]. The highest quality myrrh comes from *C. myrrha* (Nees) Engl.; this myrrh can also be under the synonyms *Commiphora rivae, Commiphora coriacea, C. molmol,* and *Commiphora habessinica* [16]. In addition, many oleoresin resins are produced by different *Commiphora* species, which resemble myrrh and are sometimes used to adulterate it [33]. One challenge in myrrh studies is that many market samples cannot be traced to their plant sources, making it difficult to identify adulteration in commercial myrrh [24], [34]. A warm balsamic, sweet, and somewhat spicy aroma characterizes myrrh, with a sharp, bitter, and astringent taste when fresh [35]. This characteristic aroma is due to furanosesquiterpenes, which possess various therapeutic properties, including hypoglycemic, antifungal, anesthetic, and antibacterial effects [29], [31], [33]. These furanosesquiterpenoids have been identified by several methods using gas chromatography/mass spectrometry, including isofuranogermacrine, lindestrin, furanoiodesma-1,3-diene, and furanodine [28], [33], [36]. Dehydropyrrocorzirinone also exhibits a resinous myrrh-like odor. The presence or absence of these compounds can detect adulteration of commercial myrrh resins [16]. Myrrh has been recognized as an important resource in folk medicine in various cultures, including Egypt, China, and Greece [20]. It has been used to treat various ailments, including inflammatory diseases, coronary artery disease, gynecological conditions, and obesity [15]. It is used topically to treat ulcers, abscesses, wounds, headaches, backaches, fungal infections, muscle pain, spasms, and snakebites [37]. In addition, myrrh is used for its medicinal and aroma properties and is the source of Balsam of Mecca, as well as Balm of Gilead [12]. The main use of myrrh is as incense in religious rites, whereas its resin is distilled to produce volatile oils for perfumery [35]. The United States Food and Drug Administration (U.S. FDA) gave its stamp of approval for a natural flavoring that is safe for use in food, drinks, and cosmetic products [22].

This review aims to provide a comprehensive analysis of *C. myrrha* (myrrh) throughout its history, geographic distribution, taxonomic profile, chemical composition, extraction methods, isolation, and phytochemical analysis. It also has traditional uses, biological and pharmacological activities, toxicity, and safety indices. Through this review, we will try to discuss the medical use of myrrh at a safe dose and, finally, a scientific outlook on its use in therapeutics and industry.

2. REVIEW METHODOLOGY

This review was conducted following a structured and systematic approach to collect, evaluate, and synthesize existing scientific literature related to *C. myrrha*. A comprehensive literature search was carried out using the following electronic databases: PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. The search

covered publications published up to December 2024. The keywords used included combinations of terms such as: "*C. myrrha*", "myrrh", "phytochemicals," "phytoconstituents," "essential oil," "extraction methods," "biological activity," "therapeutic uses," "Gas Chromatography–Mass Spectrometry (GC-MS), "toxicity, "and "ethnopharmacology. " The inclusion criteria were articles written in English, peer-reviewed journals, review articles, original research, theses, and scientific reports directly related to *C. myrrha*. Studies focusing exclusively on other *Commiphora* species were excluded unless relevant comparative data were provided. The selected studies were critically evaluated and categorized into thematic sections, including botanical characteristics, traditional uses, extraction methods, chemical compositions, and biological and pharmacological activities. The goal was to identify knowledge gaps, summarize the current findings, and propose future research directions. This methodological approach ensured a balanced, evidence-based synthesis of existing data that aligned with the objectives of a high-quality scientific review.

3. HISTORY

In cultural and religious ceremonies, myrrh and frankincense were used as incense, as recorded in ancient times [27], [38]. Yemen has historically been a major producer of frankincense, which is used extensively in traditional medicine [39]. The Arabian Peninsula is known as the original cradle of herbal medicine, with folk remedies and the use of myrrh dating back thousands of years [5]. Historical texts, including the Bible, refer to the widespread use of myrrh resin, highlighting its cultural significance [40]. For example, myrrh has been used by the Greeks and Sumerians to treat many ailments, including worms, stomach pain, and flatulence, especially in children [41]. Myrrh was considered more precious than gold and was given to Jesus at birth, as recorded in biblical tradition [1], [20]. Myrrh was an offering that the Magi brought to Jesus when he was born. The recorded medicinal use of myrrh in Chinese medicine dates back to 600 AD, during the Tang Dynasty. Its use for wound healing, pain relief, and management of menstrual cramps continues in various cultural practices [16], [42]. Around 3,000 BC, myrrh trade in ancient Egyptian mythology described these resins as "Tears of Horus," as the most vivid accounts show. One such instance of this trade is Queen Hatshepsut's voyage to the land of Punt, about 1700 BC [43]. These precious resins were exported to regions such as Rome, China, and North Africa, as later texts of Roman, Greek, and Indian origin recount. The domestication of camels made it possible to ship these resins across the desert regions of the Arabian Peninsula by 1100 BC [44]. Both myrrh and frankincense are mentioned in the Gospel of Matthew, where the Magi presented these gifts to young Christ. They were highly valued in ancient times, especially in southern Arabia, where they were an important source of wealth [38]. The burning of myrrh incense is often performed in Christian, Jewish, and Orthodox religious settings [17]. Historical accounts indicate that Greek soldiers carried myrrh compresses to treat wounds in battle [29]. The Queen of Sheba connected her visit to King Solomon by bringing balsam, a rare and precious substance similar to myrrh. After Judea's conquest, Pompey brought it to Rome. Romans used balms. During Vespasian's destruction of Jerusalem, it became a war [16]. It is worth noting that the most renowned Muslim physician, Al-Razi, utilized myrrh to treat problems of the kidney and bladder, as well as swelling [16]. Jewish tradition also considered myrrh oil sacred, and both the Old and New Testaments mention "vinum murratum," or wine mixed with myrrh, as being offered to Christ before his crucifixion. The Gospel of St. Mark also refers to this [16]. Myrrh is an essential incense with other uses such as medicine. It was exported via the so-called "Incense Route" to civilizations such as Ancient Egypt, Greece, or Rome. The extensive network of trade throughout myrrh's extensive geographical area indicates the value these kingdoms placed on this natural resource to elevate their political, economic, and cultural status. Findings from archaeological excavations and Sabaean inscriptions show that trade in myrrh and frankincense created international links between ancient Yemen and the major countries of the ancient world [45].

4. DISTRIBUTION

The Burseraceae family comprises 20 genera [38]. There are more than 150 species of *Commiphora* genus [43]. *Commiphora* is a pantropical genus that grows well in arid and semi-arid regions [20], [46], [47]. *Commiphora* occurs in Iran, Pakistan, the Arabian Peninsula India, Sri Lanka, Brazil [48], and Madagascar, with few species occurring in South America [42], and is also distributed around the Red Sea [16], east Africa [49], Somalia [16], north Africa, Kenya, and Tanzania [46]. There are seven [50] and eight [12] to 12 [49] species of *Commiphora* in Yemen, distributed in Al-Mushrifah, southern Hays, Ma'rib, Hajjah, Lawdar, Mudiyah, Ahwar, Hadhramaut, Shabwa, Socotra, and Al-Mahra [50]. Four species of the myrrh genus *Commiphora* (Burseraceae) are endemic to Socotra Island [49]. Yemen, Saudi Arabia, Oman, Somalia, Eritrea, Kenya, and eastern Ethiopia are native to this species [18]. Most of the world's myrrh is found in Somalia, and the largest market for the resin and the largest importer of myrrh is the People's Republic of China, which is used primarily in traditional medicines [16], [42].

Figure 2. *C. myrrha* gum in nature [20].

5. DESCRIPTION AND TAXONOMICAL PROFILE

Large bushes and small trees of the genus *Commiphora* (Burseraceae) grow to a height of three meters. The stem had large, sharply pointed thorns, rounded crowns, robust trunks, and dark brown bark. The plant has several spiny, asymmetrical, stunted stems [43], [46]. The shrubs had deciduous leaves and many twigs, with or without thorns. The leaves in *Commiphora* are ½ inch long [27] unequal, and pinnately alternate or fascicled compound, petiolate, or seated (or very rarely unifoliolate). Many species have spine-armed, 1–3 (or more) foliolate, imparipinnate leaves. Leaflets are either sessile or subsessile, serrated, crenate, or entire. Moreover, they are in the terminal panicles [15], [48], [50]. Bark is often exfoliated, divided into scales or flakes, and contains cleavage canals and lysine cavities. It peels off into thin sheets to reveal a colored and sometimes photochromic bark beneath [48], [50], filled with a yellowish, granular, resinous fluid [50]. The dioecious flowers are small, often red or yellow, solitary or clustered, 2-5 or small racemes, sessile, bisexual, or unisexual. The flowering season is late spring [15], [20]. The fruit is a drupe, spherical or sub-spherical, compressed or not, lanceolate, and usually has a two-chambered ovary (one aborted) [15], [50]. In native species in drier environments, stems are often succulent [48]. *C. myrrha* Engl., commonly known as myrrh, is a flowering plant classified under the domain Eukarya and kingdom Plantae within the subkingdom Viridiplantae. It belongs to the phylum Tracheophyta, subphylum Radiatopses, and the infraphylum Euphyllophytina. Taxonomically, it falls under the class Spermatopsida, subclass Rosidae, and order Sapindales within the superorder Rutanae. It is a member of the family Burseraceae and genus *Commiphora*, with the specific epithet *myrrha*, making its full botanical name *C. myrrha* Engl [15].

6. ECOLOGY AND BIOGEOGRAPHY

Ecological studies of species are essential for understanding organisms in all possible spheres [51]. The color of myrrh and the proportions of the compounds in a sample are influenced by climatic and environmental

Figure 3. *C. myrrha* [20].

conditions, which lead to variations in its appearance and cause myrrh to exhibit a range of colors, including red, orange, yellow, brown, and black [16]. *Commiphora* is found across the tropics and thrives under arid and semiarid conditions [47]. The shrub grows in very hot and sunny places at an altitude of 1500-3000 ft [27]. It usually occurs most frequently in low-scrubby vegetation and shallow soils [15]. All *Commiphora* species can be found in rocky habitats such as hills, steep slopes, or mountain slopes. These regions usually have shallow drought-prone soils and igneous rocks, such as granite or basalt. The elevation range for these habitats spans from 80 m to 1200 m above sea level. *C. myrrha* and other species of the genus have not been found in deep-soil inland or coastal plains, but have been discovered in tough, coarse pink granite combined with granodiorite and gray diorite [47]. The altitudinal ranges, average annual rainfall, and pedological and soil parameters at which *C. myrrha* prefers to grow are listed below.

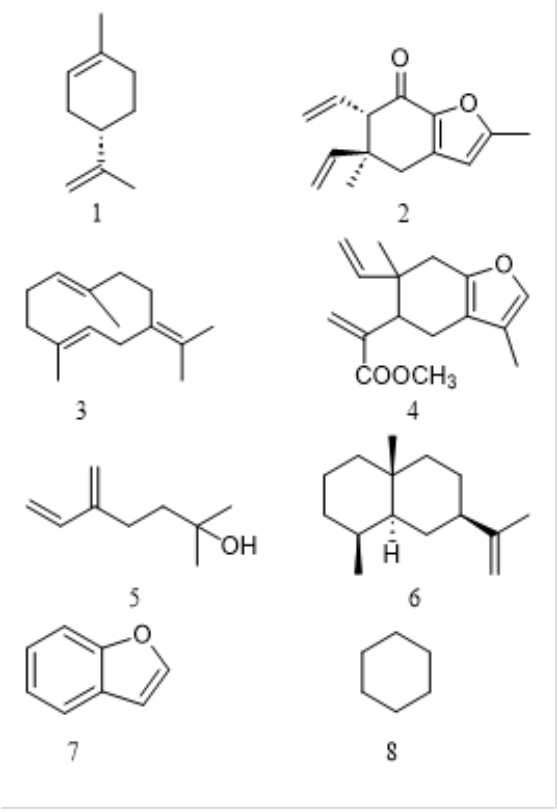
7. PHYTOCHEMICAL STUDIES

The spectral profile of myrrh was very different from those of the other resins examined. The reason for this difference is mainly the relatively high content of gum, which causes spectral changes. As a result, myrrh can be easily distinguished from other resins, especially diterpenoid and triterpenoid resins, based on its spectra [16]. The oleo-gum resin of *C. molmol* possesses polysaccharides, proteins [52], and other secondary metabolites, including tannins, polyphenolics, flavonoids, terpenes, alkaloids, and saponins [31]. Terpenes are mainly sesquiterpenes

Table 1. parameters registered where C. myrrha grows

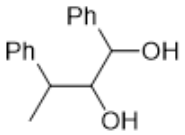
Parameter	value	Parameter	value	Reference
Coarse sand %	5.6	HCO_3^- (mg//Kg)	79.0	[47], [48]
Fine sand %	79.3	K^+ (mg//Kg)	3.40	
Silt %	10.9	Na^+ (mg /Kg)	4.30	
Clay %	4.2	Mg^{2+} (mg/Kg)	39.1	
pH	7.50	Ca^{2+} (mg /Kg)	41.0	
Conductivity (mS/cm)	1.43	Topography	Mountain slops	
SO_4^{2-}(mg/Kg)	135.0	Altitude range (m)	250–1200	
Cl^- (mg//Kg)	110.1	Geological substratum	Coarse pink granite mixed with diorite	
Altitudinal range in m	250 - 1300	Annual Rainfall in mm	250 - 350	

(isoprenoids, i.e., terpenoids), notably furanosesquiterpenes [25], [31], based on eudesmane, 10, elemane 11, and germacrene 12 compounds [52]. It contains heerabolene [29] (probably tricyclic sesquiterpene) [16], elemol 35, cadinene 28, cuminaldehyde 16, eugenol 17, and numerous furano-sesquiterpenes, such as furanodienone 18, furanodiene 19, curzerenone 2, and lindestrene 20. Compounds 2-methoxyfuranodiene 21 and 2-acetoxyfuranodi-ene 22, which belong to the furanosesquiterpenoid family, gave a positive Ehrlich color test with p-dimethylamino-benzaldehyde reagent, indicating the presence of a furan ring [29], and were isolated from *C. myrrha* gum [20]. Analysis of the methanol extract of *C. myrrha* whole plant powder revealed the presence of tannins, flavonoids, glycosides, terpenoids, saponins, alkaloids, and phenolic compounds [6], [53]. The gas chromatography-mass spectrometry (GC-MS) method of myrrh ethanolic extract was used to estimate a considerable number of 27 chemical compounds, including limonene 1, curzerene 84, germacrene B 3, isocericenine 4, myrcenol 5, β-selinene 6, spathulenol 7, and others [54].



According to the Gas Chromatography–Mass Spectrometry (GC-Ms) data from another study, 48 compounds were obtained. The oil components were compared with those in the library (NIST) based on the retention index and mass fragmentation patterns. The highest percentage compounds were 29.13%) 7, followed by 19.88% Cyclohexane 8, and 17% 1,3-Diphenyle-1,2-butanediol 9 [55].

However, considerable levels of several inorganic elements were found in myrrh resin using Inductively Coupled Plasma Mass Spectrometry (ICP-MS) to identify 62 inorganic elements. Large concentrations of Mg, Cr, Ca, Al, Br, phosphorus, Cl, and scandium been reported [54].



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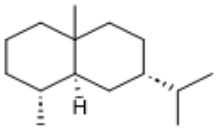

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7.1. Terpenoids

7.1.1. Monoterpenoids, sesquiterpenoids, and volatile oil

Terpenoids, mainly sesquiterpenoids and triterpenoids, are the chief constituents of *Commiphora species* [56] Chemical research is underway to isolate sesquiterpenoids, diterpenoids, triterpenoids, and lignans from the gum resins of *C. myrrha* [38]. Volatile oil mainly contains monoterpenoids, which have been identified using gas chromatography-based methods [42]. Low-oxidation sesquiterpenoids are the main components of the volatile oils. Many sesquiterpenoids, including β-elemene 23, α-copaene 24, α-humulene 25, β-selinene 26, and germacrene B3, are found in the volatile oils of various *Commiphora* species [42]. In the genus *Commiphora*, the primary families of sesquiterpenoids in the genus Commiphora are germacrene 12, eudesmane 10, guaiane 27, cadinene 28, elemane 11, bisabolene 29, and oplopane [52]. A study by Shen et al.. al. (2009) reported the presence of the sesquiterpenoid myrrhanolide A 50 and myrrhanolides B and C (34 and 49, respectively). In addition, hydroxylindestrenolide 33, 8-hydroxyisogermafurenolide 14, myrrhone 73, curzerenone 2, (1E)-3-methoxy-8,12-epoxygermacra-1,7,10,11-tetraen-6-one, (1E,2R,4R)-2-methoxy-8,12-epoxygermacra-1(10),7,11-trien-6-one 105, rel-(1S,2S,4R)-epoxyfuranogermacr-10(15)-en-6-one 95, 2-methoxy-5-acetoxyfurano- germacr-1(10)-en-6-one 78, and 4a-methoxy-6-guaien-10a-ol were identified by comparing their Nuclear Magnetic Resonance (NMR) and Mass Spectrometry (MS) data with previous reports in the literature [57].

7.1.2. Diterpenoids

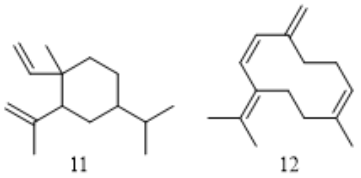
Two abietane diterpenoids, dehydroabietic acid 32 and abietic acid 31, and a pimarane diterpenoid, sandaracopimaric acid 30, have recently been identified in *C. myrrha* [42].

7.1.3. Triterpenoids

Commiphora kua, *Commiphora dalzieli*, *Commiphora confusa*, and *C. myrrha* are among the four *Commiphora* species whose resins have been shown to contain over twenty-one dammarane triterpenoids [42]. The largest group of triterpenoids identified in *Commiphora* species is dammarane triterpenoids [57]. Cycloartane-1α,2α,3β,25-tetraol (neomyrrhaol) 57 is a novel cycloartane-type triterpene that has been discovered in *C. myrrha* [15] along with four other known terpenes: sandaracopimaric acid 30, abietic acid 31, 2-methoxy-5-acetoxyfruranogermacr-1(10)-en-6-one 58, dehydroabietic acid 32 [58], and myrrhasin [57].

7.2. Steroids and flavonoids

Compounds such as flavonoids are present in the stems, bark, and flowers of this genus, but not in the resinous exudates. The species *Commiphora mukul* is the only one that contains steroids, including nine cholestane and eleven pregnane steroids [53].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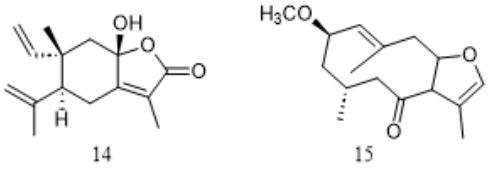

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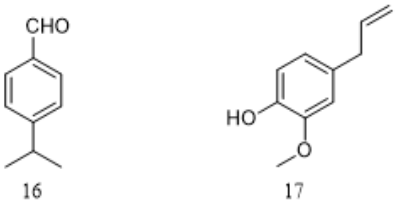

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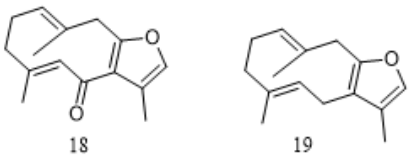

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8. MYRRH-*COMMIPHORA* CHEMISTRY

Over the years, various taxonomists have identified the *Commiphora* genus. A lot was written by different authors like Berg, Engler, Sprague, Chiovenda, Burtt, Leenhouts, Wild, Van der Walt, Gillett, and Boulos in the 19th and 20th centuries, between 1862 and 2000 [48]. Myrrh is composed of volatile oil, resins that dissolve in alcohol, and gum that dissolves in water. Polysaccharides and proteins are present in gum, whereas terpenes, sterols,

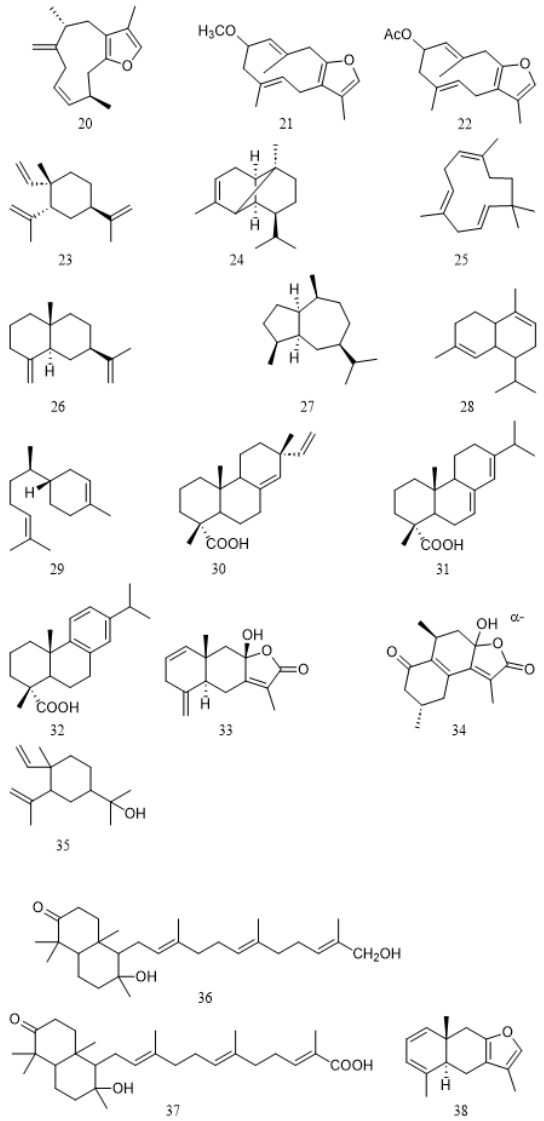
and steroids make up the volatile oil, which makes up the lipophilic myrrh component [22]. According to investigations, myrrh includes approximately 40–60% gum, 23–40% resin, and 2–8% essential oil (myrrhol) [18], [46], [59], including acidic polysaccharides such as galactose, 4-O-methylglucuronic acid 39, and arabinose 40 [46] associated with the enzyme oxidase [60], 2 to 4% impurities, and 10 to 25% bitter principles [27], [49]. Other constituents include flavonoids, alkaloids, tannins, glycosides, saponins, and terpenoids (sesquiterpenes and furanosesquiterpenoids) [27].

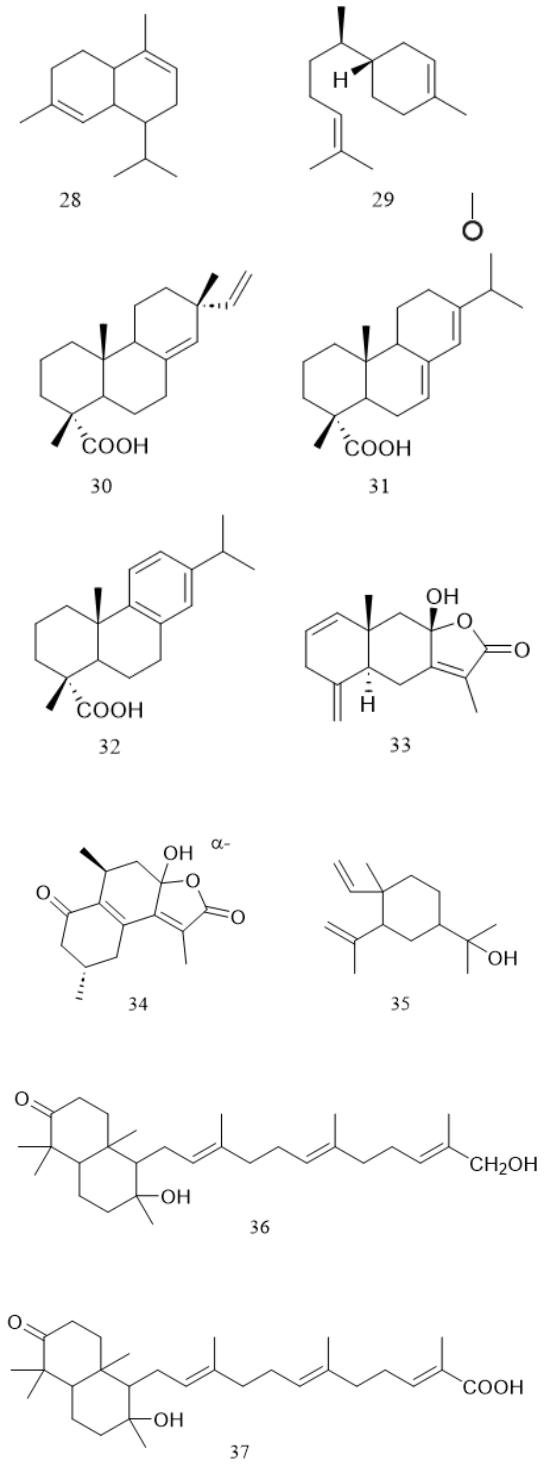
Figure 4. *C. myrrha* resin [32]

8.1. Chemical constituents of Volatile oil

The volatile oil of C. molmol is typically obtained using hydrodistillation. It exhibits reddish-brown [22] or deep amber coloration [28], often described as having a woody, spicy, bitter, and smoky aroma [19]. Interestingly, pale-yellow oil develops a violet tint upon contact with bromine vapors or nitric acid fumes [22]. Chemically, oil is dominated by terpenoids and terpenes, notably sesquiterpenes and monoterpenes, including α-, β-, and γ-bisabolenes. These collectively comprise 2–10% of the oil's mass and are considered responsible for its distinct aroma and biological effects [8], [31], [55]. The chemistry of myrrh oil was first explored by Loewensohn (1906), von Friedrich (1907), and Douroux and Trost (1936), who identified key components such as herabolene 13, cadinene 28,α-pinene 40, limonene 1, cuminaldehyde 16, cinnamic aldehyde 41, eugenol 17, and m-cresol 42. Additionally, acids like acetic, formic, palmitic and merolic acid $(C_{16}H_{21}O_3COOH)$have also been detected, along with bicyclic and tricyclic sesquiterpenes $(C_{15}H_{24})$ [24], [61]. A hallmark of C. myrrha oil is the abundance of furanosesquiterpenes, including furanodiene 19, furanodienone 18, curzerenone 2, lindestrene 20, and furanoeudesma-1,3-diene 38 [22], [25]. These compounds are frequently cited as the most bioactive constituents, and are used as chemotaxonomic markers. Further GC-MS analysis reported secondary metabolites, such as elemol 35, commipherol 36, commipherin 37, and β-elemene 23 [1], [62]. One study reported the following major constituents: furanodiene 19 at 19.7%, furanoeudesma-1,3-diene 38 at 34.0%, lindestrene 20 at 12.0%, β-elemene 23 at 8.4%, and 2-O-acetyl-8,12 epoxygermacra-1(10),4,7,11-tetranene 68 [19], [56]. A GC-MS analysis of hydrodistilled oil revealed 48 volatile compounds, with benzofuran 7 accounting for 29.13%, followed by cyclohexane 8 at 19.88%, and 1,3-diphenyl-1,2-butanediol 39 at 15.17% [63]. Using SCFE- CO_2 extraction and GC-MS, furanoeudesma-1,3-dione reached 31.1%, curzerene 84 reached 23.1%, and germacra-1(10),7,11-trien-15-oic acid, 8,12-epoxy-6-hydroxy-γ-lactone 14.4%, with lindestrene 20 contributing 11.9% [62]. Khalil et al. (2020) identified furanoeudesma-1,3-diene 38 as 15.99% and 2-acetoxyfuranodiene 22 as 26.82% in hexane and essential oil extracts, respectively [4]. In another study examining six C. myrrha samples, furanoeudesma-1,3-diene 38 consistently ranged between 29.4% and 51.5%, demonstrating both its chemical dominance and variability among sources [17]. Additional compounds reported by Lebda et al. (2021) include elaidic acid methyl ester (43.52%), eugenol (11.96%), sitosterol (17.57%), and thunbergol (11.32%) [64]. GC-MS analysis of C. myrrha grown in China showed that the oil comprised mainly monoterpenes, sesquiterpenes, alcohols, and esters, notably 2-cyclohexene-1-one, β-elemene, and copaene [11]. The chemical composition of C. myrrha volatile oil is influenced by several crucial factors, including geographic origin, plant age, extraction techniques, and postharvest processing. These variables introduce significant fluctuations in the relative abundance of key constituents, such as furanoeudesma-1,3-diene 38, curzerene 84, and β-elemene 23, despite their consistent identification across studies. Such variability presents challenges to comparability, reproducibility, and standardization of results. In addition, most existing studies are largely descriptive, focusing on the chemical identification of compounds, without establishing clear links to biological activities. There is a notable lack of toxicological, pharmacokinetic, and dose-response data, which are essential for therapeutic validation. Another gap lies in the under-investigation of minor constituents and potential synergistic interactions between components, which may contribute significantly to the overall pharmacological profile of the oil. The absence of unified analytical protocols further complicates these limitations. To overcome these issues, future research should adopt standardized extraction and analytical methodologies, incorporate bioactivity-guided fractionation, and examine the influence of environmental and geographical factors

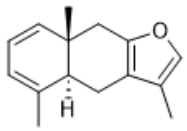
on the phytochemical profiles. These steps are necessary to enhance the scientific rigor, clinical relevance, and pharmaceutical potential of C. myrrha volatile oils.





8.2. Chemical Constituents of Resin

C. myrrha resin is up to 40% [27] is incompletely elucidated [29] but it is generally classified into a bigger ether-soluble fraction that consists of α-, β-, and γ-commiphoric acid 55, esters of a resin acid, commiphorinic acid, and two phenolic resins, α- and β-heerabomyrrhol, and a smaller insoluble fraction that contains α- and β - β-heerabomyrrholic acids [18], [27], [64] Moreover, it contains heeraboresene, commiferin 56, keto steroids, compesterol, β-sitosterol, cholesterol, α-amyrone 47, 3-epi-α-amyrin 46 [59], [64] acetate, 3-epi-lupenyl acetate 44, lupeone 45, acetyl β-eudesmol 48, a sesquiterpenoid lactone [59], isolinalyl acetate 43 [16] and myrrhanolides B and C (34 and 39, respectively) [57]. It exhibits a fluorescent spot on thin-layer chromatography (TLC), likely due to the formation of dehydroabietic acid 32 [29]. It also includes diterpenoids such as sandaracopimaric acid 30, abietic acid 31, dehydroabietic acid 32, and triterpenoids such as 3-epi-α-amirone 46, mansumbinone 53, 3,4-seco-mansumbinoic acid 54, steroids, lignans [30], myrrhasin 51, and myrrhanolide A 50 [57]. The analysis of myrrh ethanol extract by GC and GC-MS techniques showed the presence of 59 components comprising 95.3 % of the total oil composition. Myrrh extract is a reddish-brown, viscous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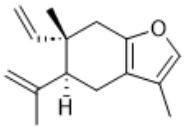
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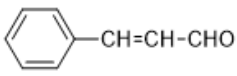
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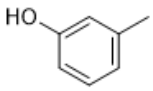
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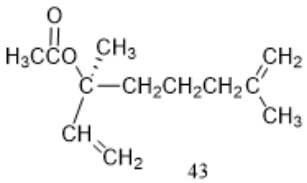
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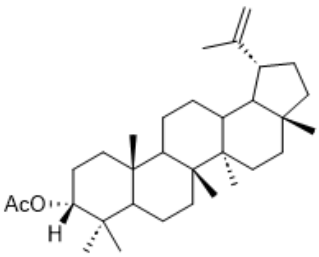
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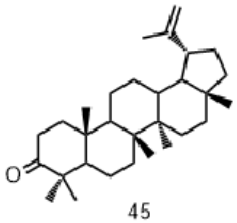
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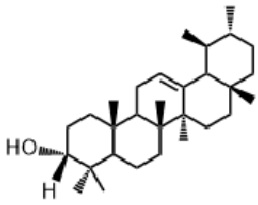
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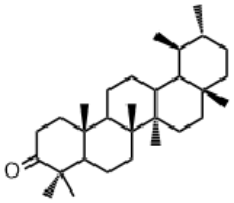
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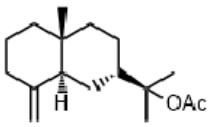
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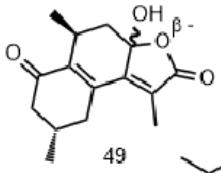
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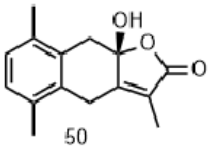
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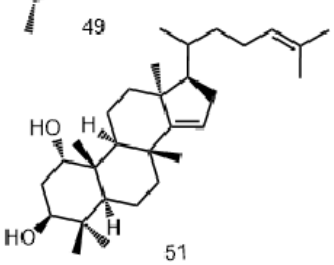
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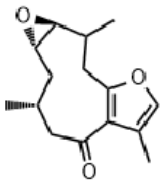
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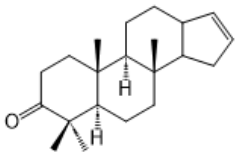
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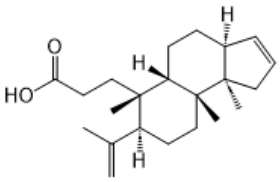
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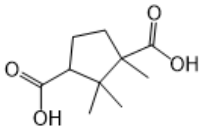
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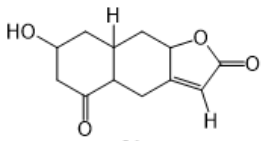
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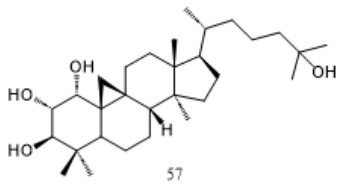
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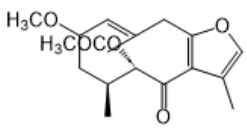
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mass substance that has a warm, balsamic, sweet, aromatic odor with a flash point higher than 93C°. The primary constituents of the extract of myrrh ethanol were 2-tert-Butyl-1,4-naphthoquinone 89 (25.9%), 3-methoxy-α-phenylbenzenemethanol 86 (7.7%), and curzerene 84 (5.8%) [28].

8.3. Chemical Constituents of Gum

C. myrrha gum up to 60%, and the crude gum from the alcohol-insoluble matter (i.e., water-soluble) *C. molmol* contains 18% protein and 65% carbohydrates as d-galactose 60, l-arabinose 61, d-glucuronic acid 62 [29], [46], long-chain aliphatic derivatives [22], and ash [30]. The gum has an oxidase enzyme associated with it [15], [18] and consists of polysaccharides, which, upon hydrolysis, yield a variety of sugars. Structure 59 of gum was established by Wiendle and Franz [31].

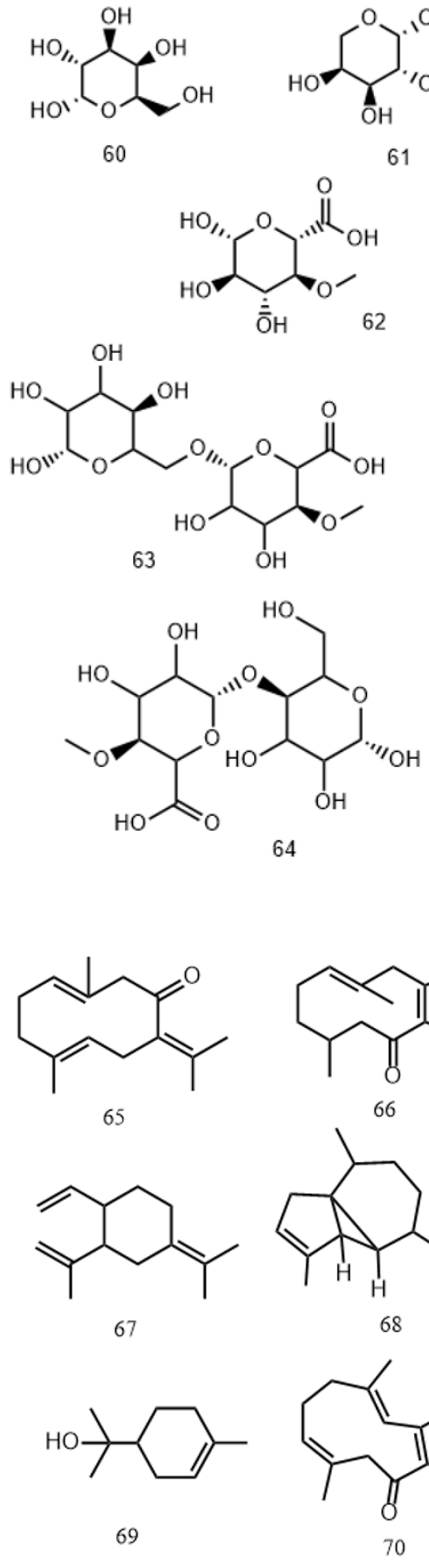
4-OCH3- α-GlcAp-$(1 \rightarrow 4)-\beta$-Galp-$(1 \rightarrow 3)$ - β - Galp-[$(1 \rightarrow 2)$-4-OCH3- α-GlcAp-$(1 \rightarrow 4)$ - β - Galp]6-$(1 \rightarrow 4)$ - α-Araf- $(1 \rightarrow 3)$ Araf $(1 \rightarrow 2)$-Araf - $(1 \rightarrow 4)$-DL-Hyp 59

GlcAp = D-Glucopyranosyluronic acid

Galp = D-Galactopyranose

Araf = L-Arabinofuranose

Hyp = 4-Hydroxypyroline [29].



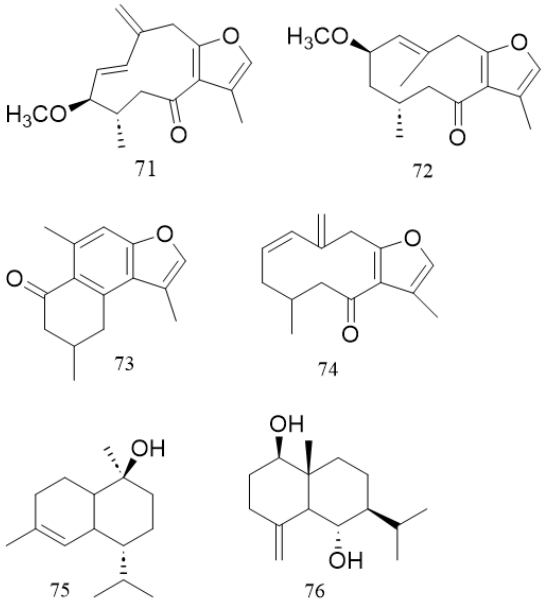
9. EXTRACTION

The resins are extracted using organic solvents, and the product is referred to as a “resinoid or an absolute used in the fragrance industry. The “absolute” is obtained by using alcohol to extract the resins whereas, the “resinoid” is prepared by use of hydrocarbon solvents such as hexane or petroleum ether to extract the crude resin. The first product contained nearly all the available essential oils of the resin. In contrast, essential oils are separated by steam or hydrodistillation at atmospheric pressure [21]. These various extraction techniques, as shown in Table 2, ranging from traditional maceration to advanced supercritical CO_2 extraction, reflect the growing interest in optimizing the yield and bioactive compound recovery from *C. myrrha*. However, differences in solvents, extraction times, and plant parts tested can lead to variations in the phytochemical profiles, underscoring the need for method standardization in comparative studies.

10. ISOLATION:

Approximately 300 molecules have been identified within the *Commiphora* genus, with extensive documentation and isolation of metabolites from various species, as reported by Hanuš et al. (2005) and El-Ashry et al. (2003) [42]. Among these, *C. myrrha* and *C. molmol* have been widely studied for their complex chemical profiles, with samples collected from diverse geographic locations, including Yemen, Saudi Arabia, Kenya, Ethiopia, and China [67].

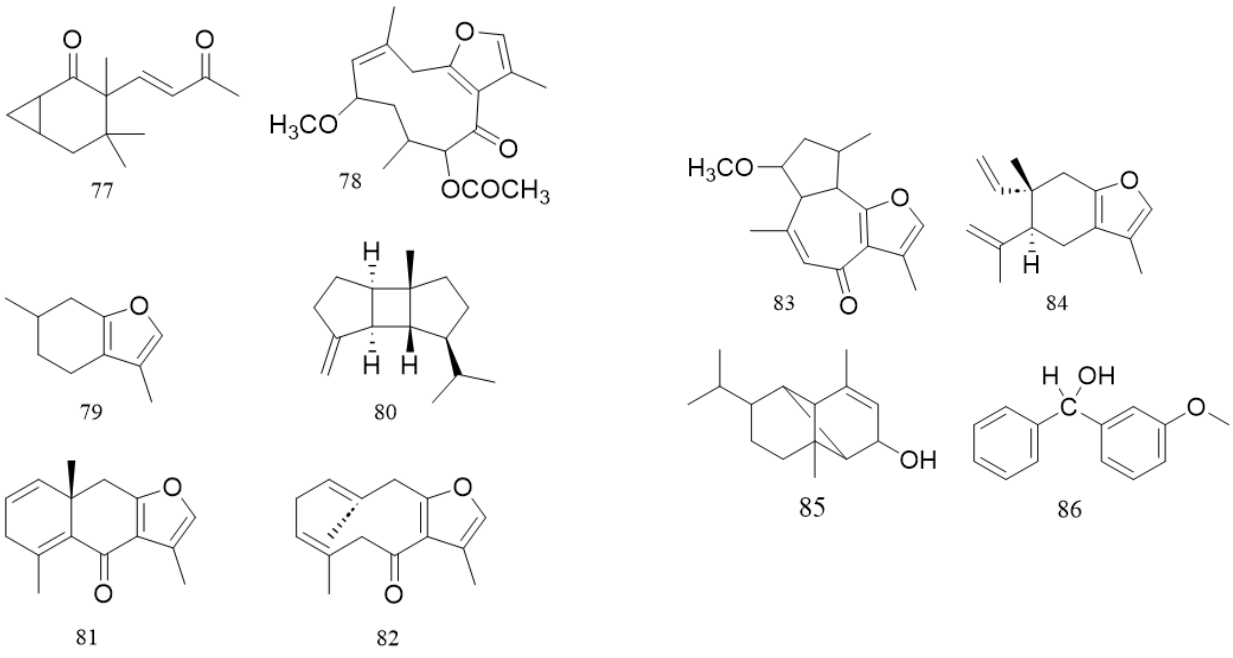
Furanosesquiterpenoids are a major class of bioactive compounds that have been isolated from *C. myrrha*. Notably, 2-methoxyfuranodiene (2-O-methyl-8,12-epoxygermacra-1(10),4,7,11-tetraene) 21 and 2-acetoxyfuranodiene (2-O-acetyl-8,12-epoxygermacra-1(10),4,7,11-tetraene) 22 have been identified in ethanolic, hexane, and chloroform extracts [67]. Other significant furanosesquiterpenes include furanoeudesma-1,3-diene (38), furanodiene (19), 4,5-dihydrofuranodiene-6-one (66), curzerenone (2), and furanoeudesma-1,4-diene-6-one (81), which have been consistently isolated across samples from different regions [67].



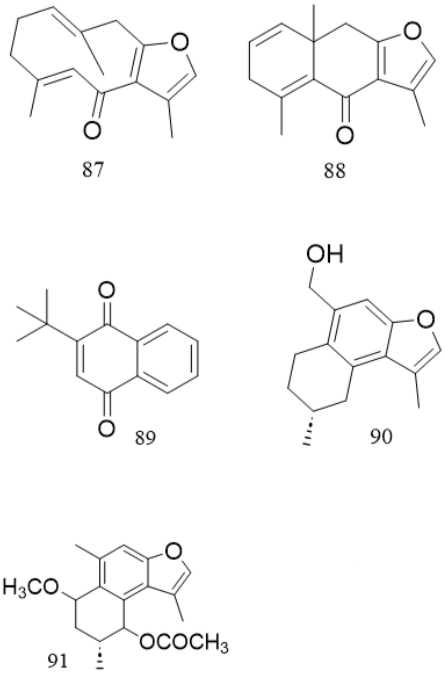
Beyond furanosesquiterpenoids, several sesquiterpenes and terpenoids have been reported, includ-

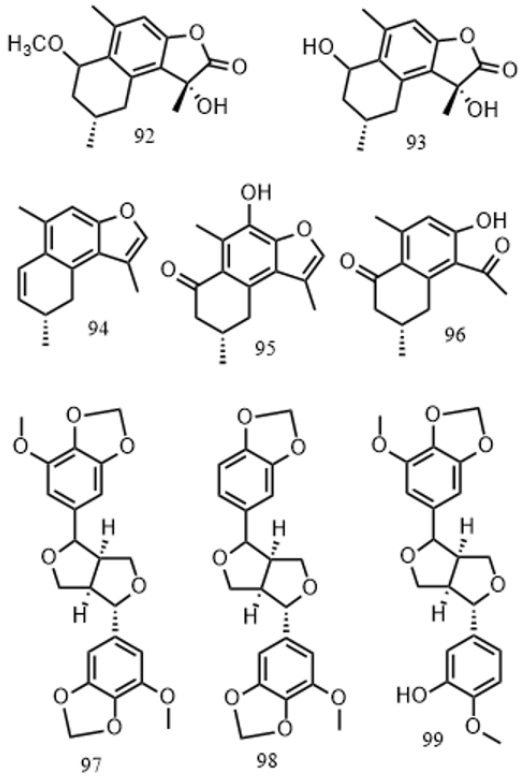
Table 2. Extraction methods and solvents used

Part tested	Method	Solvent used	Reference
whole plant powder	Soxhlet	Methanol, ethanol, water	[53]
Ole-gum resin	Hydro-distillation and maceration	H_2O and Ethanol	[28], [37]
Ole-gum resin	maceration	Ethanol	[54], [63]
Ole-gum resin	maceration	Ethyl acetate, n-hexane, ether, ethanol, and a mixture of ethanol: phosphate buffer pH 7 (85:15)	[49]
Ole-gum resin	maceration	DEMSO	[31]
Ole-gum resin	Soxhlet and maceration	Water, Methanol, and Chloroform	[25]
Ole-gum resin	Sonication and decoction	Water	[19]
Ole-gum resin	Supercritical fluid extraction	CO_2	[23]
Ole-gum resin	maceration	Ethanol	[32], [65]
Ole-gum resin	shaken by ultrasonic	Distilled water	[66]
Ole-gum resin	maceration	Petroleum ether, ethyl acetate, methanol, and water	[6]
Ole-gum resin	Hydro-distillation and maceration	H_2O and hexane	[63]
Ole-gum resin	Hot maceration	Water	[18]
Ole-gum resin	Hydro-distillation	Water	[33]
Ole-gum resin	Sonication, Soxhlet and matrix solid-phase dispersion	Methanol	[60]



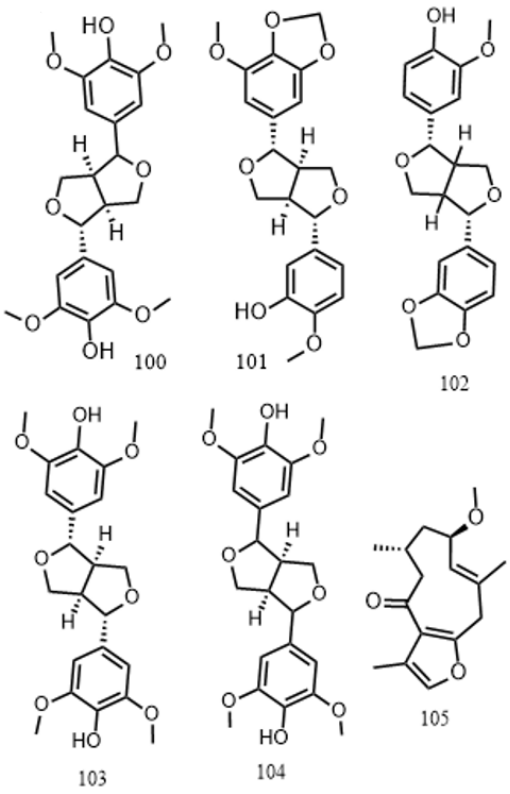
ing commiferin 56, germacrone 65, lindestrene 20, β-elemene 23, γ-elemene 67, isofuranogermacrene 39, curzerenone 2, and α-cubebene 68 [16], [29]. These compounds have been successfully isolated using various chromatographic techniques, including column chromatography on silica gel, RP-18, and semi-preparative high-performance liquid chromatography (HPLC) [16], [35]. Recent investigations have led to the discovery of new sesquiterpenoid compounds. Three novel cadinane-type sesquiterpenes, designated as commiterpenes (90–92), were isolated from the dichloromethane extracts of *C. myrrha* resin, accompanied by previously identified cadinane sesquiterpenes (93–96) [46], [68], [69]. Furthermore, eight stereoisomeric lignans, including (+)-epi-excelsin 97, (+)$-5'-$demethoxyepiexcelsin 98, and (+)-dia-syringaresinol 103, were characterized by hexane/methanol chromatography of methanolic extracts of *C. myrrha* gum resin water supernatant [22]. The water-soluble gum fraction of *C. myrrha* was primarily composed of proteoglycans, mainly uronic acid polymers. The key monosaccharides identified included d-galactose 60, l-arabinose 61, and 4-methyl D-glucuronic acid 62, along with two aldobiuronic acids-6-O-(4-O-methyl-β-D-glucuronosyl)-D-galactose 63 and 4-O-(4-O-methyl-α-D-glucuronosyl)-D-galactose 64, present in a 6:1 ratio. Additionally, approximately 15 amino acids have been detected in the gum fraction [16], [59]. The water-soluble gum fraction of myrrh is a mixture of proteoglycans, which are uronic acid polymers. A detailed account is provided of the gum myrrh (*C. myrrha* Holmes) isolation and characterization of D-galactose 60, L-arabinose 61, and 4-methyl D-glucuronic acid 62. Additionally, two aldobiuronic acids, identified as 6-O-(4-O-methyl-β-D-glucuronosyl)-D-galactose 63 and 4-O-(4-O-methyl-α-D-glucuronosyl)-D-galactose 64, were reported at a ratio of 6:1. Gums also contain approximately 15 amino acids [16], [59].





11. TRADITIONAL USES

Among all families of the plant kingdom, members of the Burseraceae have been used for centuries in traditional medicine [6], [25]. For centuries, *C. myrrha* resin has been traditionally employed as an incense [25] owing to its deodorizing properties [27]. Yemen hosts diverse medicinal flora that are used by local people for medicinal purposes [25]. Approximately 50% of the population of Yemen utilizes traditional medicine as their primary health care. Over 500 plant species have been used in the treatment of diseases in Yemen. Due to the economic conditions and large population living in rural areas, Yemenis are very interested in wild plants. According to old Sumerian manuscripts, myrrh has been used for infected teeth and worms [5]. Myrrh has been traditionally used as a natural medicine to treat various diseases, such as amenorrhea, painful dysmenorrhea



[70], tumors [71], fever, chest ailments [54], [71], stomach complaints [51], [71], gall bladder snake [32], scorpion bites [57], skin infections [54], [58], kidney diseases [65], ulcerative colitis, burn treatment [54] in ancient India, Rome, Greece, Egypt, China, and Babylon [32], [71]. *C. myrrha* In the Arab world, C. myrrha is often employed as an herbal remedy, usually as an aqueous extract from boiled gummy root for oral consumption. The most common traditional claim is the treatment of diabetes mellitus [70]. Other uses of *C. myrrha* include obesity, pain, fractures, arthritis, hyperlipidemia, cancer [19], wound injuries [31], treatment of aphthous ulcers [32], [72], gum swelling, intramucosal wounds [67], asthma, paralysis [65], incense, toothpaste [18], [51] tinctures for the treatment of gingivitis, and industrial uses such as paste and sealer. It is also used in incenses and cosmetics for skin treatment, hair, scalp [65], [73], embalming ointments [23], and gastrointestinal diseases [74]. Myrrh is used in ethnoveterinary medicine to treat skin abscesses and wounds [28]. It is an effective remedy for mouth and throat problems [18], [58] and can also help with atherosclerosis, hemorrhoids, hepatoses, hypertension, stomatitis, immunodepression, and hyperglycemia [58], [75]. *C. molmol* resin smoke is used to repel snakes and prevent respiratory infections [76].

Historically, for many centuries across generations, myrrh and frankincense have been commonly used as single prescriptions in traditional Chinese medicine. This combination has therapeutic benefits that surpass those of a single drug for treating disorders [46].

The European Council has accepted the use of myrrh in foodstuffs as per their published list of acceptable plants [77]. *C. myrrha* resin is widely used as a traditional remedy in Saudi Arabia, as per many survey studies. In 2003, a poll showed that 35 percent of 1408 healthy volunteers consumed *C. myrrha* resins within the year [19]. These traditional applications are summarized in Table 3, highlighting the region-specific uses of *C. myrrha* across civilizations.

12. PHARMACOLOGY

The primary pharmacological effects of myrrh in many modern studies are anti-inflammatory, [62] anticancer [30], [46], analgesic [80], anti-ulcer [51], anti-mutagenic, anti-diabetic [41] antimicrobial properties antischistosomal, antioxidant [32], [62], hypolipidemic [31], antiviral [27], [46], immunostimulant [27], antinociceptive [64] and antiseptic [18], [55]. *C. myrrha* helps reduce fever, purify blood, and protect the heart, in addition to its documented expectorant activity [27], [46]. Previous studies have found that myrrh is useful in the treatment of ulcers, schistosomiasis, fasciolopsiasis, respiratory catarrh, furunculosis, and diabetes. It has been observed that drug permeability from the epidermis to dermal capillaries increases in the presence of myrrh and has wound-healing properties [32]. The extract of myrrh from *C. molmol* of petroleum ether demonstrated a significant inhibition of inflammation. It also shows significant antipyretic activity in mice. Doses of myrrh (250 and 500 mg/kg/day) showed cytotoxic activity in the cells of the Ehrlich carcinoma tumor in mice [29]. Among these compounds, elemene is found in myrrh oil and is traditionally associated with improved blood circulation. It also has antitumor effects. Pinene exerts pharmacological effects. These include antimicrobial, antimalarial, antibacterial, anti-inflammatory, anticoagulant, antitumor, antioxidant, and analgesic properties [32]. Not only does the resin of the genus display antimicrobial potential, but the bark, leaf, and stem are also active against microorganisms [77]. Some sesquiterpene lactones have been used to treat several diseases. Helenalin is an anti-inflammatory drug [1].

13. BIOLOGICAL ACTIVITIES

Oleo-gum resin of *C. molmol* Engler is a biological source [15], and it has antibacterial and antifungal activities that support the traditional use of myrrh in the treatment of bacterial infections [25]. As demonstrated in the literature review, different forms of myrrh crude extract, myrrh tincture, and myrrh oil have shown antibacterial activity, and the antifungal activity of myrrh ethanol extract has been confirmed against *Candida albicans, Aspergillus flavus, A. niger, and Penicillium citrinum* [28]. *C. myrrha* has also been reported to lower fat and cholesterol levels, whereas guggulsterones are antagonist ligands [59].

Table 3. Traditional uses of C. myrrha

Place	Uses	Reference
China	For skin ulcers, wounds, fractures, oral ulcers, and toothaches. For pain, tumors, arthritis, inflammatory diseases, and diseases of blood stagnation.	[42], [63], [78]
Greece	For wounds, worms, sepsis, cough, snakebite, mouth infections, teeth, and eyes.	[31], [42], [51]
Britain	Pharyngitis, tonsillitis, gingivitis, ulcers, cough, proctitis, sinusitis, and skin inflammation.	[42]
France	as Nasal congestion caused by the common cold, small wounds, and infection of the buccal cavity.	
Germany	Oral diseases.	
America	Sore throats, oral mucosal, and gingival irritations.	
India	To treat diabetes and other inflammatory conditions. It can also help relieve fever, deal with infection, stimulate appetite, function as a mouthwash, and cure many stomach conditions including cancer.	[65], [79]
Mesopotamian	medicine as fragrance or anti-infection.	[79]
Egypt	*C. molmol* resin is available in the form of sold in the market under the commercial name Mirazid ® in Egypt and is used as an antiparasitic.	[42]
Arab World	In Arab medicine, myrrh is used for inflammation-related, stomach, and diabetes disease treatment.	[70]

Essential oils derived from plants or herbal drugs easily penetrate the cell membrane and can thus be easily absorbed from the skin and lungs [26].

Curzerene 84 was the bioactive compound that exhibited the highest toxicological activity. Methoxyfuranodiene,β-elemene 23, and α-pinene 40 also contribute to toxicology [32]. The volatile components of *C. molmol* (myrrh) exhibit antibacterial and antifungal activities against standard pathogenic strains of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* [44]. Sesquiterpenes and sesquiterpenoids, such

as sesquiterpene lactones, which are important volatile oil components, have numerous biological properties, including antibacterial, antifungal, antiviral, anti-inflammatory, and antiparasitic properties. It is also important to note that recent studies have revealed analgesic and anticancer properties in vivo as well as in vitro [22], [65]. It is also worth mentioning that recent studies have reported that the four major constituents of the oil, furanodienone 18, furanoeudesma-1,3-diene 38, curzerene 2, and β-elemene 23, showed in vivo and in vitro anticancer and analgesic activities [22].

13.1. Anti-inflammatory activity

Myrrh gum resin contains various terpenoid constituents with anti-inflammatory properties. Studies have shown that these terpenoids suppress cytokine production activated by lipopolysaccharides (LPS), including nitric oxide in mouse peritoneal cells, as well as the expression of cyclooxygenase-2, interleukin-6, interleukin-1β, and inducible nitric oxide synthase [46]. The volatile oil of *C. molmol* was also found to prevent IL-1b from stimulating IL-6 and IL-8 production in human gingival cells. *C. molmol* resin petroleum ether extract has inhibitory activity against inflammation induced by cottonseed and carrageenan [42]. An extract derived from *C. myrrha* showed anti-inflammatory activity by significantly decreasing paw edema volume. This decrease was similar to that caused by indomethacin and was likely due to the inhibition of prostaglandin (PGs) release. Furthermore, *C. molmol* myrrh appeared to have a stabilizing effect on the intestinal barrier. Therefore, *C. molmol* is used to treat an inflammatory bowel disease [46].

13.2. Antioxidants

Antioxidants are considered important bioactive components because of their numerous health benefits and key role in delaying oxidative rancidity in various foods [81]. The myrrh extracts contained many compounds, such as diterpenes, sesquiterpenoids, sterols, and triterpenes, which might serve as electron donors. These substances interact with free radicals, converting them into more stable compounds and cutting off radical chain reactions [20]. The essential oil of *C. myrrha* has antioxidant activity and can eliminate harmful reactive oxygen species in the body, such as superoxide anion radical [54] and singlet oxygen [42]. This reaction is due to the furan ring of *C. myrrha* constituents, especially furanosesquiterpenoids [15], [54] eugenol, and cinnamic aldehyde [31]. The essential oil of *C. myrrha*, rich in furanosesquiterpenoids, such as 2-methoxyfuranodiene and 2-acetoxyfuranodiene, has demonstrated significant antioxidant activity by neutralizing reactive oxygen species and protecting against DNA oxidative damage, as observed in in vitro studies and commercial sample analysis [60], [82].

On the other hand, the ethanol extract of *C molmol* was reported to exhibit antioxidant activity in an in vitro study because of its phenolic and flavonoid contents [27].

Myrrh oleo-gum resin of *C. molmol* reduces DNA damage caused by oxidative stress in the body. The myrrh oleo-gum resin significantly decreased the levels of 8-hydroxydeoxyguanosine (8-OHdG), an index that reflects DNA damage caused by oxidative stress in the body. According to a study conducted on cultured cells, the oleo-resin of myrrh can resist oxidation [31]. The Somali myrrh (Burseraceae) resin and essential oil showed quenching activity against singlet oxygen as well as DL-α-tocopherol in a study that used 1,3-diphenylisobenzofuran (DPBF) as a test agent associated with lipid oxidation and DNA degradation [15].

13.3. Antibacterial activity

The antimicrobial activity of *C. myrrha* has been evaluated using various standard methods, including the disk diffusion [49], [55], agar well diffusion [18], [65], broth and agar dilution [44], [74], micro-atmosphere assay [6] and viable count techniques [63]. The essential oil of *C. molmol* showed strong antibacterial effects against *Staphylococcus aureus*, including multidrug-resistant strains [57], [74], eliminating more than 99.999% of bacterial cells [63]. It also demonstrated activity against *S. mutans*, *Escherichia coli, Pseudomonas aeruginosa*, and *Lactobacillus spp.*, with comparable effectiveness to that of chlorhexidine gluconate [19], [55]. Arin et al. (2021) reported inhibition zones of 7.75–9.75 mm and MIC values of 12.4–49.6 µg/mL against *Salmonella spp.,* with higher efficacy against Gram-positive bacteria [26]. Additionally, the essential oil exhibited better antimicrobial performance than ethanol extracts [28] and showed growth inhibition against *Staphylococcus aureus, E. coli, and P. aeruginosa* [27]. Investigation of the action of the *C. myrrha* extract in ethanol revealed potent activity. The minimum inhibitory concentrations (MIC) of the ethanolic extract against P. aeruginosa and E. coli were 20 mg/ml against *P. aeruginosa* and 40 mg/ml *E. coli*. The ether extract was found to have a minimum inhibitory concentration (MIC) of 10 mg/ml and 40 mg/ml against *S. albus* and *C. albicans* [74]. In addition, the methanol extract examined can be considered an effective *anti-staphylococcal* [74] against *E. coli, S. aureus, K. pneumoniae*, and B. *cereus*. particularly notable against *P. mirabilis* [17] and *K. pneumoniae* because of the existence of broad-spectrum antimicrobial compounds that act against gram-negative bacteria [27]. The extract of *C. molmol* (myrrh) in diethyl ether inhibited the growth of *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae, and Enterobacter cloacae* but not *Pseudomonas aeruginosa and Serratia marcescens.* Additionally, its petroleum ether extract has

Table 4. Biological activity of *C. myrrha* components

Extract	Activity	Reference
Resin	*C. myrrha* resin, in varying amounts, was found to inhibit the growth and aflatoxin production of *Aspergillus* species. It showed a reduction in the total aflatoxin secretion of 51.9-95.7% by *A. flavus* and 46.9-92% for *A. parasiticus*.	[59]
Essential oil	Myrrh oil resists the growth of dermatophytes in 43.1-61.6%. Myrrh oil demonstrated much higher antifungal activity than that of the ethanol extract. The antifungal activities of MIC and MFC values were 25–100 and 25–200 mg/ml. It showed good anti-elastase activity.	[75]
Methanol extract	Methanol Soxhlet extract of *C. molmol* (in vivo) extracts demonstrated promising anti-*T. Vaginalis* activity.	[41]
Ethanol extract	The 12.5–27.5% ethanol extract inhibition value against dermatophytes. The MIC was 25–400 and 25–400 mg/mL, and ethanol extracts showed good anti-elastase activity.	[19]
Boiled or sonicated aqueous extracts	It becomes harmful to HepG2 cells when the concentration of the dry crude extract is more than 150 mg/ml. The HepG2 cells showed increased mRNA expression levels of CYP 2C8, 2C9, and 2C19 up to 4.0 fold.	
Matrix solid-phase dispersion (MSPD) methanol extract	It exhibited the greatest ability to kill bacteria, both gram-negative and gram-positive (156.25 μg/mL and 312.5 μg/mL, respectively and fungus 156.25 μg/ml.	[60]
Isolated cadinane type	They all showed strong effects for anti-Alzheimer's disease.	[46]
Fraction (furanodiene-6-one 38 and methoxyfuranoguaia-9-ene-8-one 83	It exhibited activity against standard pathogenic strains of bacteria and fungi. These compounds were also shown to have local anesthetic properties. They were also active against *Escherichia coli, Staphylococcus aureus and Pseudomonas aeruginosa* by showing antibacterial and antifungal activity. The MIC ranges were found to be 0.18–2.80 mg/ml. These substances can induce numbness by blocking the inward flow of sodium through membranes.	[16], [29]
2-methoxyfuranodiene 21 and 2-acetoxyfuranodiene 22	They are toxic to the larvae of Rhipicephalus appendiculatus ticks, which spread the organism that causes East Coast Fever in cattle.	[21]
2-methoxy-5-acetoxyfruranogermacr-1(10)-en-6-one (58), and dehydroabietic acid (32)	They showed high aromatase inhibiting activity with IC50 values of 0.2 μM and 0.3 μM, respectively.	[15]

demonstrated antibacterial activity against *S. aureus, E. coli, and P. aeruginosa* [27]. The hexane extract of C. *molmol* (myrrh) had a lesser effect on the growth of various bacteria, such as *E. coli Staphylococcus aureus, Bacillus subtilis, and Klebsiella pneumoniae* [18]. The aqueous extract from *C. molmol* showed no inhibitory effect against any bacterial isolates, including *Bacillus subtilis, Pseudomonas aeruginosa* [18], [25], *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Serratia marcescens, and Enterobacter cloacae.* It is noticed that *Pseudomonas aeruginosa and Serratia marcescens* were the resistant isolates to Myrrh oil and extracts [18]. However, ethyl acetate and hexane extracts of *C. myrrha* inhibit growth against different

gram-negative bacteria, whereas the methanol extract has antibacterial activity only at higher concentrations [3]. The best antimicrobial activity was found in ethanol phosphate buffer pH 7 (85:15) extract against *Streptococcus mutans and Candida albicans* [49]. Several isolated compounds have been identified with potent antibacterial activity, such as methoxyfuranoguaia-9-ene-8-one 39 and furanodiene-6-one 38 showed MIC values of 0.2–2.8 µg/mL [42], [63]. Another compound, β-elemene 23, and T-cadinol inhibited a range of bacteria with MICs of 4–256 µg/mL [63], and 3,4-seco-man-sumbinoic acid 54 showed superior activity eight times more effective than norfloxacin against Staphylococcus and enhanced the action of ciprofloxacin and tetracycline against Salmonella strains SL1344 and L10 [30]. ***Myrrha in Oral and Dental Medicine*** The primary bacterium responsible for dental decay is Streptococcus mutans [80], [83], which causes dental decay, while the presence of *Lactobacillus spp.* is responsible for the start of cavities. Myrrh oil was effective against *Lactobacillus spp and S.mutans.* Therefore, it could be a potential antibacterial agent for dental cavities [80]. In a study by Almekhlafi et al.. al. (2014), mouthwash pharmaceutical formulations containing a single active constituent extracted from Yemeni myrrh indicated that the hydroalcoholic extract of a mixture of ethanol and phosphate buffer at pH 7 with a ratio (85:15) had antimicrobial activity [80]. According to research done by Izzeldien et. al. (2021), Streptococcus mutans was found to be susceptible to four concentrations of *C. myrrha* oil. The largest inhibition zone was observed at 100 mg/mL and the MBC was 3.125 mg/ml. Additionally, Lactobacillus spp. The bacteria were treated with three doses (100, 50, and 25 mg/mL) [83]. Myrrh mouthwashes in one study showed clinical improvement in plaque reduction and parameters of gingival inflammation. Myrrh can be considered as a therapeutic agent for the treatment of gingivitis. Chlorhexidine was used as a positive control [66]. In a clinical study of Al-Otaibi et al. (2020), found that mouthwash containing myrrh is an effective method for improving oral hygiene and reducing dental plaque and gingivitis in the short term, with slight side effects, as demonstrated by the clinical study, compared to chlorhexidine [72]. Khalil et.al. (2020), in also clinical study showed that using 5% v/v C. *molmol* oil formulated in cream and mouthwash. The cream demonstrated better activity against *Pseudomonas aeruginosa* than *Staphylococcus aureus*, with 95.11% killing for *P. aeruginosa* and 86.76% killing for *S. aureus* after a 2-hour contact time [63]. Evidence indicates that *C. myrrha* shows promising antibacterial effects against key oral pathogens such as *S. mutans* and *Lactobacillus spp.*, suggesting its potential use in dental care. However, variations in extract types, concentrations, and methodologies across studies limit direct comparisons and clinical translation. While some clinical trials have reported positive short-term outcomes, larger, standardized studies are needed to confirm the long-term efficacy, safety, and optimal formulations.

13.4. Neuroprotective effects

The Alzheimer's disease (AD) pathological model in Caenorhabditis elegans was screened for 90,93,95 and 96 cadinene-type sesquiterpene compounds for anti-Alzheimer's disease (AD) activities. They all exhibited significant anti-AD activities, according to the results [69]. It has been shown that three novel cadinane sesquiterpenes isolated from *C. myrrha* 90-93 have neuroprotective effects against MPP+-induced neuronal death in SH-SY5Y cells [68].

13.5. Anti-acetylcholinesterase activity

The species most widely used in Mesopotamia for the production of essential oils used in aromatherapy is *C. myrrha* (Nees, England). The methanolic resinous extract of the leaves and bark of *C. myrrha* can inhibit acetylcholinesterase (AchE) by approximately 17.00%, 26.00%, and 29.33%, respectively, compared to eserine [79]. *C. myrrha* contains bioactive components that have a good binding capacity to key sites of AchE, ranging from -5.8 (m-cresol) to -10.5 (abietic acid) kcal/mol [20], [79].

13.6. Antiparasitic activities

The *C. molmol* extract exhibits schistosomiasis [84] and antischistosomal , molluscicidal, and fasciolicidal activities, which have been thoroughly investigated and provide sufficient evidence for its use as an antiparasitic agent [42], [85]. In addition, Mirazid® was found to have a therapeutic effect in mice infected with Giardia lamblia, with a 100% reduction in both intestinal and fecal parasite numbers [43]. In Egypt, myrrh became an antiparasitic drug in 1990, supported by scientific evidence [28]. Myrrh is currently produced and used as a gelatin capsule (Mirazid®) containing 300 mg of pure *Commiphora* extract [85]. Although *C. molmol* extracts show promising antiparasitic effects supported by preclinical studies, there is a need for more extensive clinical trials to confirm their safety and efficacy in humans.

13.6.1. Myrrh as a schistosomicide

According to several studies, myrrh exhibits antischistosomal activity against various Schistosoma mansoni stages. The effect of the drug was most pronounced on days 21 and 45 post-infection in infected mice. It also had a promising prophylactic effect when administered five days before infection. The final formulation, "MirazidTM, " was prepared from different mixtures of oil, gum, and resin of myrrh [42], [84]. Mice infected with

Schistosoma mansoni are a good model for screening drugs for their possible schistosomicidal activity; in mice, the worm can develop to maturity in a reasonable length of time, produce viable eggs, and are readily available in large numbers and at low cost. Overall, mirazid was effective against S. pneumoniae misconduct. In mice, compounds with a high therapeutic index have been found to be effective against mansoni [84].

13.6.2. Myrrh as an anti-heterophyid agent

Mirazide emulsion also demonstrated remarkable activity on heterophyidiasis in an animal study, significantly reducing the number of worms, along with deformation and erosion of membranous spines, as observed under a scanning electron microscope. It was found to be highly effective, resulting in a 100% reduction in worm counts when administered at a 500 mg/kg/day dose for three consecutive days [20], [86].

13.6.3. Myrrh as a molluscicide

The anti-molluscicidal potential of myrrh was investigated on snail species Bulinus truncatus, Lymnaea cailliaudi of Egypt, and Biomphalaria alexandrina. The snail species and their eggs were exposed to various concentrations of the drug over 24 and 48 h at temperatures ranging from 22 ℃ to 26℃. The results showed that B. truncatus had (95 mg/L and 55 mg/L) and L. cailliaudi (85 mg/L and 50 mg/L) after 24 hours of exposure, which were lower than B. Alexandrina had an LD90 and LD50 of 195 ppm and 155 ppm, respectively. A 100% mortality rate for egg clutches of L. cailliaudi and B. Alexandrina was recorded at 75 ppm and 100 ppm, respectively. Reports have indicated that under laboratory conditions, noticeable inhibition of myrrh appeared on intermediate hosts of snails, particularly their eggs. The extract showed molluscicidal activity against schistosome snail hosts, with noticeable effects after 24 h of exposure [20].

13.7. Anti-cancer properties

Crude extracts of different *Commiphora* species, such as *C. mukul* and *C. myrrha*, have been studied for their antiproliferative properties against tumor cells [42]. Essential oil extraction was tested on human liver cancer (HepG2), human colon cancer (HCT-116), and colon cancer cell lines (MCF-7) to demonstrate its activity. The essential oil exhibited activity against MCF-7 with IC_{50} 10.93 ± 0.32 μg/ml [63] decreases the cell viability of human gingival fibroblasts and epithelial cells at a concentration above 0.0025% and 0.001%, which is classified as the highest recorded activity [87]. In vitro tests demonstrated the potential of the hexane extract in human liver cancer (Hep G2), human breast cancer (MCF-7), and colon cancer cell lines (HCT-116) [63], [82]. Shoemaker et al. (2005) reported that an aqueous extract of *C. myrrha* resin inhibited the growth of eight distinct tumor cell lines *in vitro*. These include A549 (human lung carcinoma), LLC (murine Lewis lung carcinoma), Panc-1 (human pancreatic carcinoma), Panc02 (murine pancreatic carcinoma), MCF-7 (human breast adenocarcinoma), MCNeuA (murine breast carcinoma), PC-3 (human prostate adenocarcinoma), and LNCaP (human prostate carcinoma). Moreover, it was also tested against cultured mammary epithelial cells of normal humans (huMEC) and failed to achieve an IC_{50} value, indicating that *C. myrrha* aqueous extract is moderately inactive in normal cells [88]. In addition, we tested the effects of aqueous extracts of *C. molmol* on HepG2 cells, a cancerous liver cell type in humans. They found that when treated with extracts ranging from 1 to 30 mg/ml, the cells showed a notable increase. The ratios of P450-12C8, 2C9, and 2C19 mRNA were up to 4.0-fold. Furthermore, this was compared to untreated control cells. In conclusion, sonicated or boiled *C. myrrha's* extracts altered the gene expression of cytochrome P450 2C8, 2C9, 2C19, and 3A4, and the extract concentration did not matter [19]. *C. molmol* resin demonstrated antitumor activity in Ehrlich solid tumor-bearing mice in vivo. The doses used were 500 and 250 mg/kg/day. The cyclophosphamide drug is used as a standard for comparison of antitumor properties for C. *molmol* resin [89]. Using MTT assay of cytotoxic, both 2-methoxyfuranodiene 21 and 2-acetoxyfuranodiene 22, compounds displayed auspicious activity against (MCF-7) breast cancer cells and liver (HepG2) with IC_{50} values of 4.4 and 3.6 μm, respectively [60]. In addition, two chemical compounds attenuated the effects of hormone non-hormonal treatment. 2-methoxy-5-acetoxyfuranogermacr -1(10)-en-6-one 58 and 71 were shown to alter binding to the ligand-protein Androgen Receptor (AR). Moreover, it interferes with the binding of ligands to the AR and alters the recruitment of the coactivators ARA70 and SRC-1 and/or suppresses AR nuclear translocation [90]. In a clonogenic test, furano-sesquiterpenoid rel-1S,2S-epoxy-4R-furanoge -rmacr-10(15)-en-6-one 95 showed less cytotoxic activity against the MCF-7 breast tumor cell line [91]. The active constituent with anticancer activity in *C. myrrha* is β-elemene 23, which has demonstrated activity against glioblastoma and various other cancer cells. Additionally, it has been confirmed to be both safe and effective. β-Elemene 23 has been shown to have anti-proliferative activity through the activation of p38MAPK in glioblastoma [30], [92]. In vitro tests on A2780, SK-OV-3 Ishikawa cell lines showed the ability of *C. myrrha* 85% EtOH extract and petroleum ether extracts to significantly inhibited cell proliferation in a dose-dependent manner. Additionally, the two new compounds that were successfully isolated, abietic acid 31 and dehydroabietic acid 32, showed dose-dependent cytotoxic effects on A2780, SK-OV-3, and Ishikawa cancer cells. Thus, extracts and compounds from myrrh could be useful for the prevention and treatment of hu-

man gynecologic cancer [93]. Daily doses of 125 or 250 mg/kg *C. molmol* resin extract for 14 weeks protected rats from diethylnitrosamine/phenobarbital-induced liver cancer, according to the findings of Mahmoud et al. (2005) [58]. Although various studies have highlighted the anticancer potential of *C. myrrha* extracts and compounds, most of the evidence remains limited to in vitro or animal models. There is a lack of human clinical trials, and the exact mechanisms of action are not yet well established.

13.8. Antidiabetic activity.

Myrrh extract helps cure digestive disorders and control levels of diabetes mellitus [65] Various studies have shown that *C. myrrha* lowers blood sugar levels and raises insulin levels in diabetic animals. The mechanism by which *C. myrrha* helps control glycemia [85]. One study aimed to investigate the antidiabetic activity of *Commiphora* extract in adult male albino rats. The use of myrrh as a potential aid in lowering high blood sugar levels was investigated in an experimental study involving diabetic rats. The report indicated that administering a dose of myrrh at 75 mg/kg body weight proved effective in reducing blood sugar levels and contributing to weight gain in rats [58]. The activity was tested at different concentrations and was 50 % for different mixtures of honey, *C. myrrha*, and Nigella Sativa against bacterial isolates taken from diabetic food of three patients [44]. The consumption of furanosesquiterpenes 22 and 81 at 150-175 µg/g of body weight from clear Gummi *myrrha* resin reduced the level of blood glucose in diabetic obese mice [94]. The extract of myrrh effectively increased glucose tolerance in both diabetic and normal rats, and consumption of 10 ml/kg of Gummi *myrrha* resin water extract per day for 7 days decreased the level of blood glucose in diabetic rats [95]. Intake (0.5-10 g/L) from the *C. myrrha* resins and in a concentrated form caused high insulin secretion, as observed after administration of the mice islands to *C. myrrha* (0.1-10 g/L), from insulin secretion. Insulin secretion from both human and mouse islets rapidly and reversibly increased after the intake (2 mg/ml) of *C. myrrha*. Consequently, the resin solution of *C. myrrha* directly stimulates Langerhans β-cells [85].

13.9. Anti-obesity activity.

Obesity is a major public health concern associated with an increased risk of metabolic disorders including diabetes mellitus, hypertension, and cardiovascular diseases [96]. *C. myrrha* promotes lipid reduction by increasing fatty acid oxidation and lipolysis [97]. The ability of *C. myrrha* to lower cholesterol and modulate immunity is important for protection against infectious disease protection [46]. A high-fat diet increases glucose levels in the body and weight. *C. myrrha* reduces body fat. These metabolites help improve liver oxidative production, liver tissue damage, and increase protein expression [96]. Notably, *C. myrrha* administration in obese rats significantly reduced body weight, blood glucose levels, atherosclerosis index, and altered lipid profiles, potentially owing to bioactive compounds such as guggulsterone and plant sterols [27].

13.10. Antifungal activity

The methanolic extracts of *C. myrrha* oleo-gum resin demonstrated concentration-dependent antifungal activity against several dermatophyte species. The mycelial weight decrease of the fungi was directly proportional to the extract concentration. The most effective in inhibiting the Epidermophyton *floccosum*, growth with a 2 g fresh mycelial weight, was the 200 g/L concentration of *myrrha,* while the least inhibition was observed in *Candida albicans*, where the fresh mycelial weight was 6.61 g at the concentration of equal extract. The methanol extract yielded the highest values for *Trichophyton concentricum* [25]. The inhibitory effect of ethanol extract against dermatophytes was 12.5–27.5%, respectively. The MIC and MFC values of the ethanol extract ranged from 25 to 400 g/L and from 25 to 400 g/L, respectively [28]. Both the ethanolic extract and essential oil of *C. myrrha* have demonstrated antifungal effects *in vitro*. The essential oil was effective against *M. canis, M. gypseum, T. mentagrophytes, T. verruscum*, and *T. rubrum*, with furanoeudesma-1,3-diene (38) and menthofuran (79) identified as the key active compounds. Conversely, the antifungal activity of the ethanolic extract was attributed to compounds such as 2-tert-butyl-1,4-naphthoquinone, 3-methoxy-α-phenylbenzene methanol, and curzerene (84) [16]. Petroleum ether and methanol extracts of oleo-gum resins from *C. myrrha* revealed antifungal activity against *Aspergillus* species: *A. flavus, A. fumigatus, A. terreus*, and *A. niger* in an in vitro study [27]. Another study reported that *C. molmol* essential oil exhibited strong antifungal activity, particularly against *Fusarium solani, Fusarium oxysporum, Cladosporium sp.*, and *Aspergillus flavus* [63]. The *C. myrrha* oil inhibitory effect against dermatophytes ranged from 43.1% to 61.6%. The MIC and MFC values of myrrh oil were 25–100 g/L and 25–200 g/L, respectively. Consequently, the ethanol extract exhibited lower antifungal activity than myrrh oil [28]. A combination of furanodiene-6-one 38 and 2-methoxyfuranoguaia-9-ene-8-one 39 was shown to exhibit anti-microbial activity against *E. coli, S. aureus, P. aeruginosa, and C. albicans* with MICs ranging from 0.18 to 2.8 g/L [98].

13.11. Analgesic activity

The analgesic activity of *C. molmol* has been demonstrated in rats, likely due to its bioactive components that enhance the pain threshold via central and peripheral

mechanisms [27]. Germano et al. (2017) found that myrrha extract, rich in furanodiene and curzerene, significantly reduced pain symptoms in male and female volunteers [99]. Key sesquiterpenes, such as furanoeudesma-1,3-diene and curzerene, act on central opioid receptors, as their effects are reversed by naloxone, suggesting opioid-mediated mechanisms [30]. Additionally, extracts of *C. myrrha* (ethanol, petroleum ether, and aqueous suspension) showed significant analgesic and antipyretic effects in animal models. However, the lack of an effect in the hot plate test suggests that peripheral mechanisms may dominate in some extracts [100]. Curzerene appears to be a major contributor to the observed analgesic effects [32].

13.12. Anti-dysmenorrheic activity

Myrrh extract exhibits significant anti-dysmenorrheic activity and inhibits uterine contraction and aromatase activity [27]. Khatoon et al. (2017) found that the combination of myrrh with Abhal and Muqil was effective in treating PCOD-related secondary amenorrhea. This combination triggered withdrawal bleeding and menstrual regulation because of the presence of steroids and flavonoids. In addition, myrrh contains terpenoids, phytosterols, lignans, phenolic, and saponin compounds, whereas Abhal contains glycosides and alkaloids, which have hormone-like actions in the body, causing withdrawal bleeding and menstrual regulation [101].

13.13. Antiviral activity

In a previous study, myrrh oil was shown to have antiviral activity against influenza *A Puerto Rico 8/34/H1N1 virus.* Its cytotoxic effect was also observed in cell lines used for infection [23]. Furanodienone 18 and curzerene 84 modulate viral replication and act at different steps of the viral life cycle [23], [46].

13.14. Nasal congestion effects

Traditionally, a few drops of myrrh oil are added to hot water and inhaled as steam. It has been used to treat headaches associated with nasal congestion, suggesting an analgesic effect [102]. The resin from the myrrh tree facilitated the movement of white blood cells and drainage. It has been found to destroy different types of microbes and stimulate white blood cells called macrophages [103], [104].

13.15. Against respiratory infections

For over two millennia, myrrh served as a frequent painkiller. It was also used by people to clean wounds and sores until morphine emerged in Europe [103]. Myrrh is also helpful for treating coughs and chest infections. It works by suppressing the associated inflammatory responses [63].

Can Myrrh combat COVID-19?

C. myrrha, commonly known as myrrh, is traditionally used for a wide range of therapeutic applications due to its analgesic, cytotoxic, anti-inflammatory, antioxidant, immunomodulatory, antimicrobial, anti-ulcer, hepatoprotective, and anti-tumor properties. Given its reported antiviral effects, there is growing interest in evaluating its potential against viral infections, including COVID-19. Some studies and anecdotal reports have suggested a possible role for myrrh-based preparations, such as mouthwashes, as supportive treatments during the COVID-19 pandemic [20], [105]. Furthermore, increased demand and price hikes reported in certain regions, such as Qatar, reflect public perception of myrrh's medicinal value. However, more rigorous experimental and clinical studies are needed to validate these claims and determine their efficacy and safety in COVID-19 management.

13.16. Cardioprotective activity

C. molmol protects the heart in animal models of heart attack by reducing oxidative stress and improving heart cells. In a study of myocardial infarction in rats, *C. molmol* reduced inflammatory and apoptotic activity [105].

13.17. Anticoagulant activity

Mice's platelet aggregation was inhibited by administering 100 mg/kg of Gummi myrrha resin ethyl acetate extract, while the water extract was ineffective [46]. Antithrombotic effect was shown on mice when given 100 µg/g of Gummi myrrha resin extract of ethyl acetate [106].

13.18. Wound healing activity

Using a myrrh mouthwash may have a positive effect on wound healing after tooth extraction. Wound size, postoperative surgery site edema, and discomfort are all improved with Myrrh mouthwash [107]. On the second and seventh postpartum days in primiparous women, patients who received *C. myrrha* showed a considerably better development in the healing of their episiotomy wounds compared to those who received frankincense or betadine [108].

13.19. Anti-ulcer activity

Peptic ulcers are erosions in the lining of the digestive tract [62]. Traditionally, myrrh has been used as an effective remedy for infections and is considered beneficial in treating various types of ulcers [27]. Myrrh extract was more protective and curative than myrrh oil against gastric ulcer-induced oxidative alterations caused by ethanol [109]. Ulcers were induced in rats using 80% ethanol, NaCl, and NaOH, and it was found that indomethacin

demonstrated dose-dependent anti-ulcer and gastric mucosa protective effects from the aqueous extract of *C. molmol* resin. The necrosis, erosion, congestion, and hemorrhage of the stomach wall induced by 80% ethanol extract were improved with *C. molmol* pretreatment [110].

13.20. Hepatoprotective effect

The treatment with *C. myrrha* induced a more normal appearance of the liver histology, which was seen in the reduction of liver enzymes aspartate transaminase (AST), alanine transaminase (ALT)) in a dose-dependent manner in rats. It boosts antioxidant activity in the liver and reduces oxidative stress through down-regulation of key players: TNF-α, IL-6, IL-10, iNOS-2, and HO-1; thereby protecting against oxidative cellular damage. The histological improvement towards normalization suggests that *C. myrrha* extract can protect parenchymal cells and enhance liver tissue regeneration. The presence of bioactive compounds like flavonoids, terpenoids, and alkaloids is responsible for their hepatoprotective effect [111]. As per the report, the activities of reduced glutathione, glutathione S-transferase, and glutathione peroxidase were lowered in the PbAc-intoxicated rabbit model; recovery was observed on treatment with the resin of *C. molmol* [112].

14. TOXICITY

Toxicological studies on *C. myrrha* have revealed that its safety largely depends on dosage, route of administration, and duration of use. While therapeutic doses are generally well tolerated, higher concentrations may pose risks. High doses of *C. myrrha* resin have shown adverse effects in animals [113]. One goat died following oral administration of 1–5 mg/g/day [42], while in mice, the LD_{50} of Mirazid solution was recorded at 3139 mg/kg [114]. Acute signs of toxicity in rats included huddling, jaundice, hepatonephropathy, and hemorrhagic myositis when administered intramuscularly at 500 mg/kg/day or intraperitoneally at 250 mg/kg/day. However, no mortality was observed in mice administered 3 g/kg of total ethanolic extract [46]. In addition, owing to the emmenagogic properties of myrrh, miscarriages have been reported in women who apply a high dose during pregnancy [115]. Allergic reactions have also been reported [15]. Myrrh is generally not suggested for patients with a hot constitution. It is a naturally occurring flavoring substance (which has been approved by the United States Food and Drug Administration (U.S. FDA) [42]. In a research study, the safety of myrrh was assessed after an overnight fast, and the agent was administered orally at a dose of 11.5 mg/kg for three days [77]. In people without infection, tests for liver and kidney function showed that normality was maintained at weeks 1, 2, 4, and 8 post-treatments. Meanwhile, no notable side effect were observed [42]. In a comparable study, the drug was administered at a dose of 10 mg/kg for 3 to 6 days with mild and transient adverse effects [116]. Another study administered mice with 500 mg/kg myrrh extract for five successive days and noted no evidence of hepatotoxicity after 12 weeks post-treatment [42]. An animal model (rat) was used to compare the genotoxicity, hepatotoxicity, and carcinogenicity of three materials: which extract of myrrh, formulation of Mirazid, and praziquantel as a standard drug. Bilirubin level, ALT, and AST level in serum, histopathology of liver, and bone core cell-cytogenetic studies were assessed. six successive weeks, myrrh was administered once daily with an amount of 500 mg/kg, while praziquantel was given at 1500 mg/kg once weekly. Based on the study, praziquantel has genotoxic, carcinogenic, and hepatotoxic properties. However, Myrrh was found to be safe with no genotoxic, carcinogenic, and hepatotoxic properties [117]. This study supports earlier results on safety, which may be due to chronic usage. When myrrh and cyclosporine were used together, cyclosporine was less available for absorption in rats [118]. The researchers assessed the acute toxicity of gummi *myrrha* by taking information from the oral intake of gummi myrrh resin for 24 h and whether it causes any mortality in groups of mice. Some chronic toxicities were also tested for the last 90 days. In the chronic study, the body weight and weights of the testes, cauda epididymis, and seminal vesicles increased in treated animals compared to the controls. Treated animals exhibited higher red blood cell counts and hemoglobin levels. Treated animals did not exhibit spermatoxic effects [64]. Crude extracts of the resin of *C. myrrha* were subjected to an acute toxicity study using Swiss albino mice. The 1.2 g/kg doses of *C. myrrha* extract was non-toxic. These results were also compatible with those of Rao et al. (2001), where the resin of *C. myrrha* water extract did not show any visible signs of toxicity in mice at a dose of 3 mg/g [76]. *C. myrrha* has demonstrated a favorable safety profile at therapeutic doses in multiple studies. However, caution should be exercised with high concentrations, specific routes of administration, pregnancy, and potential drug interactions. Standardized dosing and clinical guidelines are essential for safe use.

15. PRECAUTIONS OF GUMMI *MYRRHA*

Although major drug interactions have not been clinically reported, Gummi *myrrha* might interfere with the action of antidiabetic drugs and lower blood glucose levels through resin action. Patients on anticoagulant medication should consult their healthcare professionals before taking the resin [46]. The water extract of gummi myrrha resin at a dose of (40 mg/plate) exhibited no mutagenic activity in a *Salmonella/microsome* assay using *Salmonella typhimurium strains* [36]. The Gummi *myrrha* water extract resin, which is injected into the abdominal cavity at 10-40

times the normal therapeutic dose, has no mutagenic effect [106]. The water extract of the resin at 40 mg per plate was able to inhibit the extra mutation of aflatoxin B1 in the Salmonella typhimurium strain. Lactating mothers and children should avoid the Gummi myrrha unless recommended by a licensed healthcare practitioner [46].

16. GUMMI *MYRRHA* DOSE

Gummi myrrha has a variety of forms, including capsules, powdered resin, myrrh tinctures, and topical ointments. Gummi *myrrha* must be kept in direct sunlight and in a well-sealed container. The undiluted tincture was applied to the affected site two or three times a day. The mouth rinse solution was prepared by adding five–10 drops of tincture to a glass of water. The mouthwash solution was prepared by adding 30-60 drops of tincture to a glass of warm water. Ointment formulations are applied directly to the affected gums or oral mucosa using a brush or cotton swab, two or three times per day. Additionally, dental powders containing 10% powdered gum resin may be used as an oral hygiene supplement [46].

17. REVIEW LIMITATION

Despite the extensive historical and contemporary interest in *C. myrrha*, several limitations persist across the existing body of research. One major constraint is the lack of standardization in extraction techniques, solvents used, and analytical methodologies, which leads to significant variability in chemical composition and bioactivity outcomes. This inconsistency makes it difficult to compare results across studies or reliably reproduce the findings. Furthermore, although a large number of chemical constituents have been isolated and identified, particularly sesquiterpenes and furano-type compounds, the biological significance of many minor metabolites remains unclear, with limited studies addressing their pharmacodynamic or synergistic effects. Another critical gap is the paucity of clinical trials and in vivo models. Most pharmacological and toxicological findings are based on in vitro or animal studies, which limits the ability to translate these outcomes into validated human therapeutic applications. Moreover, toxicological profiling and dose standardization are largely insufficient or inconsistent across studies. Few investigations assess the long-term safety, bioavailability, or pharmacokinetic profiles of individual compounds or whole extracts. In addition, the ethnobotanical uses of myrrh are well-documented, but many traditional claims lack rigorous scientific validation, and the socio-cultural contexts of use are underexplored. To bridge these gaps, future studies should emphasize standardized protocols, conduct well-designed clinical trials, explore structure–activity relationships, and perform toxicological risk assessments to support the safe and effective use of *C. myrrha* in modern medicine.

18. CONCLUSION

In this review, *C. myrrha* has traditionally been used as a medicinal plant. Recent studies have confirmed its phytochemical properties and biological activities, including antimicrobial, anti-inflammatory, antioxidant, anticancer, and antidiabetic effects. Its essential oils, resins, and gums offer remarkable therapeutic potential, mainly due to the presence of terpenoids and flavonoids. Although myrrh has been extensively used, scientific exploration of its pharmacological use has not been performed on a large scale in clinical trials beyond its historical use. This review highlights the considerable promise of *C. myrrha*. There is an emerging trend of the inclusion of *C. myrrha* in the cosmetic and pharmaceutical industries. In addition, there are some gaps in research, there are some gaps in the research, such as the bioavailability of active compounds, toxicity, and drug interactions. The methods used by researchers for isolating and testing the bioactive components of myrrh differ from one another, making it difficult to compare results. To develop a standardized extraction protocol and study the pharmacokinetics of *C. myrrha*, future in vivo studies should be conducted . In addition, ethnopharmacologists, natural product chemists, pharmacologists, and clinical researchers have an excellent opportunity to collaborate in a multidisciplinary manner to achieve complete therapeutic potential. studies in different geographic locations would provide a different picture of the phytochemical variability and biological activity of C. *myrrha*. There may be different plant chemotypes based on the growth habitat and environmental conditions. Further attention should also focus more on the physiological effects of C. *myrrha* and explore how it interacts with other drugs and whether it can be used to augment current therapy regimens, particularly for chronic diseases. In summary, *C. myrrha* is a novel candidate for natural products. This can be used for novel agent development because it is bioactive and has several properties. To fully realize this authenticity, more rigorous scientific verification, including clinical and preclinical investigations, is necessary. Therefore, *C. myrrha* has a bright future in pharmacology and drug development to sustainably produce plant-based therapies. Research in different countries can help us learn more about the distinct chemical plants produce and whether they have health benefits.

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