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Review

Myrrh: A Resin of Ancient Tradition at the Service of Science

Abstract

The resinous exudates of *Commiphora myrrha*, known as 'myrrh', are used in Traditional Chinese Medicine for the treatment of trauma, arthritis, fractures and other diseases. The isolated metabolites and crude extracts of myrrh have exhibited a wide of *in vitro* and *in vivo* pharmacological effects, including antiproliferative, antioxidant, anti-inflammatory and antimicrobial activities. Myrrh has also been used in the ayurvedic medical system because of its therapeutic effects against inflammatory diseases, coronary artery diseases, gynaecological disease, obesity, etc.
Expansion of research materials would provide more opportunities for the discovery of new bioactive principles from the genus *Commiphora*.

Maria Cristina Marzano [1]

Rosalì Amelotti [1]

Rudy Ferretti [2]

[1] Revalma Inc Srl Società Benefit

[2] Rode pharma Srl

*Corresponding author:
Author: Maria Cristina Marzano

c.marzano@revalma.com

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Introduction

The repetitive use of drugs to treat many diseases can cause various side effects. This has led to a search for medicinal herbs as alternative medicine. Medicinal herbs have been used around the world since ancient times [1]. The World Health Organization reports that 90% of the world's population relies on traditional medicine [1, 2]. Yet, natural medicinal extracts can be more viable, cheaper, and safer compared to synthetic drugs.

Commiphora myrrha (Nees) Engl., also known as Balsamdendron Myrrha and *Commiphora molmol*, is a plant species of the genus *Commiphora*, from the family Burseraceae. Its primary distribution is semi-arid and arid areas, including southern Arabia, northern Somalia, India, Sudan, northern Kenya, and Ethiopia, growing at an altitude of 1500–3000 feet in very hot and sunny areas [2, 3, 4, 5].

The word myrrh is derived from the Arabic 'murr' meaning bitter, and its functions have been documented in the writings of Hippocrates since the time of ancient Rome. In fact, it is believed that myrrh was among the three presents that the Magi gave to the infant Jesus [6]. Moreover, it was reported that Greek soldiers would not go to battles without a potion of myrrh to place on their injuries [4].

Myrrh is the resin derived from making incisions in the stem of the plant, causing oleoresin to exude and dry as it is extracted from the plant. Indeed, the phloem includes schizogenous tubules that are filled with yellowish fine grained resinous fluid and lysigenous cavities. The leaves are around half an inch long, and there are no flowers.

Myrrh has a range of applications and benefits, including anti-inflammatory properties and many infectious diseases treatments, and is becoming a very popular and valuable alternative medicine [4, 5]. Its extracts have been used to cure wounds, ulcers, and different diseases of the respiratory, gastrointestinal and urinary tract [7]. It has also been proven to be effective against HSV-1 infections and microbial activity, demonstrating its successful use in conventional treatments for aerosolised therapy for the treatment of bronchitis and sinus infections [3, 8].

Moreover, the resinous exudates of the genus *Commiphora* are commonly used as perfume, incense, or embalming ointment [9].

Chemical constituents

Myrrh contains 3% – 8% essential oil, 30% – 60% water-soluble gum and 25% – 40% alcohol-soluble resins [10].

Phytochemical investigation previously resulted in the isolation and identification of many metabolites including terpenoids, steroids, flavonoids, lignans, carbohydrates, and long chain aliphatic alcohol derivatives from the *Commiphora* species [11, 12, 13, 14, 15, 16].

Terpenoids

Monoterpenoids and sesquiterpenoids

It was observed that the composition of volatile oil from different *Commiphora* species varies largely. Monoterpenoids mainly occur in volatile oil and identified by GC (gas chromatography) based techniques. Monoterpenoids, including a-pinene, camphene, b-pinene, myrcene and limonene, have been detected. Sesquiterpenoids, including b- germacrane, eudesmane, guaiane, cadinene, elemane, bisabolene and oplopane groups, have been detected. The structures of sesquiterpenoids from the genus *Commiphora* are mainly classified into more than twenty furanosesquiterpenoids, covering furanogermacrane, furanoeudes-

manes, furanoguaiane, furanocadinane and furanoelemane, since the first isolation of furanosesquiterpenoid from C. molmol [5, 17].
The presence of furanosesquiterpenoids is characteristics of this genus.

Diterpenoids

Recently, a pimarane diterpenoid and a racopimaric acid and two abietane diterpenoids – abietic acid and dehydroabietic acid – have been reported from *C. myrrha* [16].

Triterpenoids

Triterpenoids are major constituents isolated from *Commiphora* species, covering dammarane, polypodane, octanordammarane, cycloartane, oleanane, lupane, ursane, and lanostane. Recently, ten cycloartane triterpenoids with novel substitution at C-2 position have been isolated from *C. opobalsamum* and *C. myrrha* [14, 15, 16].

Miscellaneous

In *Commiphora* species, many other secondary metabolites are encountered such as carbohydrates, flavonoids, lignans and long chain aliphatic derivatives. Carbohydrates have been reported from the gum of *Commiphora*, and commonly exist in the form of polysaccharide [18, 19, 20]. Acid hydrolysis of the gum produces mono-ordi-saccharides. The flavonoids of this genus are found in the flower, stem and bark, but not obtained in the resinous exudates. 1,2,3,4-tetrahydroxy long chain aliphatic derivatives occur in the gum, for instance, D-xylo-guggultetrol-18 and guggultetrol-20 [21], which commonly exist in the form of ferulic acid esterorglycoside [14, 22].

Pharmacological activity

Anti-inflammatory activity

Myrrh and its compounds are highly effective in the treatment of inflammatory diseases. Indeed, myrrh interacts with the anti-inflammatory activity MAPK (mitogen-activated protein kinase) pathway by blocking all the synthesis of genes that lead to the production of inflammatory enzymes [23]. In this study, scientists evaluated the effects on Adjuvant-induced Arthritis (AIA) in rats. The results stated the elevated expression levels of TNFα, PGE2, IL-2, NO, and malondialdehyde (MDA) in serum; swelling in the paws of AIA rats was significantly decreased after treatment with myrrh in a manner comparable to results from the use of indomethacin. The authors found that, in mechanistic terms, myrrh reduced the inflammatory cascade, mainly TNFα-mediated, through the down-modulation of the specific transcription factors c-jun and c-fos.

The anti-inflammatory action of myrrh was also clinically evaluated in adults diagnosed with ulcerative colitis. Myrrh, in this case administered by mouth together with chamomile and activated charcoal, has shown clinical efficacy comparable to mesalazine in terms of measured score, relapses during therapy, and side effects. The effect on intestinal markers of pathology (calprotectin, lactoferrin and elastase of polymorphonuclear cells) – typically non-subjective parameters – clearly demonstrates the powerful anti-inflammatory role played mainly by myrrh. It is possible, in fact, to exclude the action of chamomile as it has recently (2018) been described as useful in the treatment of ulcerative colitis but only in the guise of its known anti-anxiety role [24].

Analgesic activity

One of the most important pharmacological activities described for myrrh is the opioid-related analgesic action. In the study of Dolara *et al*. (1996) [25], the authors isolated furanoeudesma-1,3-diene, curzerene and furanodiene from myrrh. They then reproduced abdominal pain through the writhing test. Fura-

noeudesma-1,3-diene was shown to be at least as effective as morphine in reducing painful abdominal contractions triggered by the administration of acetic acid. The effect was cancelled out with the administration of naloxone – an opiate antagonist. The same effect, and its cancellation in the presence of naloxone, was again demonstrated in the hot plate test. These data demonstrated the morphine-like analgesic effect of myrrh. The same analgesic effect was then confirmed approximately 20 years later by another research group (Di Pierro, 2019) [26]. In this case, a clinical trial performed in adults against a placebo demonstrated the analgesic effect of myrrh. Myrrh was administered for 20 days between 200 mg and 400 mg / dose – as an extract titrated in total furanodienes – in individuals suffering from headache, febrile pain, myalgia, arthralgia, lumbosciatica and pain due to dysmenorrhoea, showed a dose-type analgesic behaviour response (therefore greater than 400 mg / day) in the absence of side effects attributable to the treatment and not highlighted even in the placebo group [26].

Antimicrobial activity

The antibacterial, antifungal and anti-protozoal effects of the myrrh derivative have been extensively investigated by numerous authors. Also attributable, albeit to a lesser extent, to aqueous extracts, myrrh has shown efficacy in contrasting the *in vitro* growth of species such as *S. aureus*, *S. pyogenes*, *E. coli*, *P. aeruginosa*, *S. enterica* and *K. pneumoniae*. The verified antibacterial action was, in some tests, comparable with what was shown, in terms of minimum inhibitory concentration (MIC), by ciprofloxacin and tetracycline [27].

The antifungal action of myrrh was also found to be extremely relevant. Particular evidence has been derived from *in vitro* tests against fungal strains that can normally create skin and scalp infections such as the genera Cladosporium, Trichophyton, Microsporum and Epidermophyon. Perhaps even more clinically relevant, the anti-candida effects directed against *C. albicans*, *glabrata*, *rugosa*, *parapsilosis*, *tropicalis* and *dubliniensis* strains were evident. These actions were pharmacologically comparable with that obtained in the control plates treated with nystatin and amphotericin B [28]. Finally, some authors investigated the antiprotozoal role of myrrh extract, highlighting, in a cohort of women with metronidazole-resistant trichomoniasis, a good clinical action against *Trichomanas vaginalis* (11 out of 13 subjects recovered from trichomoniasis thanks to myrrh). In according to this latest evidence, myrrh extract can be considered an antimicrobial that certainly has a broad spectrum of action [29]. The antibacterial role of myrrh was finally evaluated in an animal model of caecal ligation and puncture. In models of this type, the leakage of faecal material into the peritoneal cavity leads the animal to sepsis, and death, in a short time. This occurs mainly due to the enormous release of TNF-α LPS-mediated that leads the animal to septic shock. As elegantly shown by the authors, oral administration of myrrh in a dose-dependent manner abrogated the release of inflammatory cytokines (including TNF-α), and reduced the risk of sepsis, prolonging the survival of some animals and improving their survival rate [30].

Toxicity

A goat was poisoned and eventually died from the oral administration of *C. myrrha* resin at a dose of 1–5 g/kg/d. The safe dose of the resin was suggested to be 0.25/kg/d [31].

Side effects of the extract of *C. mukul* resin have been observed including mild gastrointestinal discomfort, possible thyroid problems and generalized skin rash [32]. The volatile oil of myrrh can irritate the skin, respiratory and digestive systems, and may cause an allergic response, nausea and a decrease in locomotor activity [33, 34]. For these reasons, in Traditional Chinese Medicine, myrrh is pre-treated with heat to reduce the volatile oil

content before being prescribed [35, 36].
The resin of *C. erlangeriana* is poisonous to humans and animals and used for arrow poison in Eastern Africa [37].

Conclusions

The present review discusses the phytochemical and pharmacological aspects of the genus *Commiphora*, including a detailed analysis of the literature published since 2000. Terpenoids were regarded as the major constituents in this genus. Pharmacological studies carried out on crude extracts and pure metabolites provided pragmatic documents for its traditional uses and confirm this genus as a valuable source for medicinally important molecules. Regarding the constituents contributed to medicinal values, the findings indicated that triterpenoids and diterpenoids are mainly responsible for anti-inflammatory properties, sesquiterpenoids for antimicrobial, smooth muscle-relaxing and analgesic effects. Further development of the medical uses of *Commiphora* requires some research questions to be addressed. Investigation of other plant tissue of *Commiphora* such as the stem, bark and leaf may provide research opportunities for the discovery of new bioactive principles. Validating the correlations of the ethnomedical uses, bioactive substances and pharmacological effects is of special importance, and is still the primary focus for future research. Efforts are also needed to investigate in detail the physiological and biochemical functions demonstrated by *Commiphora*, identify the individual bioactive natural products, and illustrate their mechanism of action.

References

1. Shuaib M, Ali A, Ali M, *et al*. (2013) Antibacterial activity of resin rich plant extracts. J Pharm Bioallied Sci 5(4):265
2. Shalaby MA, Hammouda AAE (2014) Analgesic, anti-inflammatory and anti-hyperlipidemic activities of *Commiphora molmol* extract (Myrrh). J Ethnopharmacol 3(2):56
3. Abdallah EM, Khalid AS, Ibrahim N (2009) Antibacterial activity of oleo-gum resins of *Commiphora molmol* and Boswellia papyrifera against methicillin resistant Staphylococcus aureus (MRSA). Scientific Research and Essays 4(4):351–356
4. Shameem I. (2018) Phytochemical and therapeutic potentials of Murr Makki *(Commiphora myrrha):* A review. Indian J Appl Res 8(9):102–4
5. Shen T, Li GH, Wang XN, *et al. (2012).* The genus *Commiphora*: a review of its traditional uses, phytochemistry and pharmacology. J Ethnopharmacol 142(2):319–330
6. Nomicos, EY (2007) Myrrh: medical marvel or myth of the magi? Holist Nurs Pract 21(6):308–323
7. Galehdari H, Negahdari S, Kesmati M, *et al.* (2016) Effect of the herbal mixture composed of Aloe Vera, Henna, Adiantum capillus-veneris, and Myrrha on wound healing in streptozotocin-induced diabetic rats. BMC Complement Altern Med 16(1):1–9
8. Alamri BM (2017) Effects of Myrrh on HSV-1 Using Plaque Assay. Thesis, University of Tabuk, pp36
9. Langenheim, JH (2003) Plants resins: Chemistry, Evolution, Ecology, and Ethnobotany. Timber Press, Portland, Oregon, US
10. Tucker AO (1986). Frankincense and myrrh. Econ Bot 40(4):425–433
11. Ahmed F, Ali M, Singh O (2006) New compounds from *Commiphora myrrha* (Nees) Engl. Die Pharmazie 61(8):728–731
12. El Ashry, ESH, Rashed N, Salama OM, *et al.* (2003) Components, therapeutic value and uses of myrrh. Die Pharmazie 58(3):163–168
13. Hanuš LO, Řezanka T, Dembitsky VM, *et al.* (2005) Myrrh-*Commiphora* chemistry. Biomedical papers 149(1):3–28
14. Shen T, Wan W, Yuan H, *et al*. (2007) Secondary metabolites from *Commiphora opobalsamum* and their antiproliferative effect on human prostate cancer cells. Phytochemistry 68(9):1331–1337

15. Shen T, Lou HX. Bioactive constituents of myrrh and frankincense, two simultaneously prescribed gum resins in chinese traditional medicine. Chem Biodivers. 2008 Apr;5(4):540-53. Chemistry & biodiversity, 5(4):540–553

16. Su, Shu-Lan, *et al*. "Isolation and biological activities of neomyrrhaol and other terpenes from the resin of *Commiphora myrrha*." Planta Medica 75.04 (2009): 351-355.

17. Brieskorn CH, Noble P (1982) Constituents of the essential oil of myrrh. Planta medica 44(2):87–90

18. Bose, S., Gupta, K. C. (1964). Structure of *Commiphora* mukul gum: Part I. Nature of sugars present and sturcture of Aldobiouronic acid. Indian Journal of Chemistry 2(2):57

19. Hough L, Jones JKN, Wadman WH (1952) Some observations on the constitution of gum myrrh. J Chem Soc (Resumed):796-800

20. Jones JKN, Nunn JR (1955) The constitution of gum myrrh. Part II. J Chem Soc (Resumed):3001–3004

21. Patil VD, Nayak UR, Dev S (1973) Chemistry of ayurvedic crude drugs Part III: Guggulu (resin from *Commiphora mukul*) – long-chain aliphatic tetrols, a new class of naturally occurring lipids. Tetrahedron 29(11):1595–1598

22. Zhu N, Rafi MM, DiPaola RS *et al.* (2001). Bioactive constituents from gum guggul (*Commiphora* wightii). Phytochemistry 56(7):723–727

23. Su S, Duan J, Chen T, *et al.* (2015) Frankincense and myrrh suppress inflammation via regulation of the metabolic profiling and the MAPK signalling pathway. Sci Rep 5(1):1–15

24. Langhorst, J, Varnhagen I, Schneider SB, *et al*. (2013) Randomised clinical trial: A herbal preparation of myrrh, chamomile and coffee charcoal compared with mesalazine in maintaining remission in ulcerative colitis – a double-blind, double-dummy study. Aliment Pharmacol Ther 38(5):490–500

25. Dolara P, Luceri C, Ghelardini C, *et al.* (1996). Analgesic effects of myrrh. Nature 379(6560):29–29

26. Di Pierro F (2019) Analgesic effects of RodeMyr®, a *Commiphora molmol* extract with a highly standardized furanodiene content. Nutrafoods 2:95–99

27. Al-Daihan S, Al-Faham M, Al-shawi N, *et al.* (2013) Antibacterial activity and phytochemical screening of some medicinal plants commonly used in Saudi Arabia against selected pathogenic microorganisms. Journal of King Saud University-Science 25(2):115–120

28. Nikolic M, Smiljkovic M, Markovic *T et al.* (2016) Sensitivity of clinical isolates of Candida to essential oils from Burseraceae family. EXCLI J 15:280

29. El-Sherbiny GM, El-Sherbiny ET (2011) The Effect of *Commiphora molmol* (Myrrh) in Treatment of Trichomoniasis vaginalis infection. Iran Red Crescent Med J 13(7):480

30. Kim MS, Bae GS, Park KC, *et al*. (2012) Myrrh inhibits LPS-induced inflammatory response and protects from cecal ligation and puncture-induced sepsis. Evid Based Complement Alternat Med 2012;2012:278718

31. Omer SA, & Adam SE (1999) Toxicity of *Commiphora myrrha* to goats. Vet Hum Toxicol 41(5): 299–301

32. Nohr LA, Rasmussen LB, Straand J (2009) Resin from the mukul myrrh tree, guggul – Can it be used for treating hypercholesterolemia? A randomized, controlled study. Compl Ther Med 17(1):16–22

33. Li L, Qu C, Zhou K. (2008) Toxicity and side effects of frankincense and myrrh. J Toxicol 22:496–497

34. Rao RM, Khan ZA, Shah A H (2001) Toxicity studies in mice of *Commiphora molmol* oleo-gum–resin. Journal Ethnopharmacol 76(2):151–154

35. Chen W, Jiang X, Jiang M (2010) Study on processing technique of myrrha. China Medical Herald 7:45–47

36. Zhang J, Zhu L (2005) Improved processing technique of myrrha. Modern Traditional Chinese Medicine 25:76

37. Habtemariam S (2003) Cytotoxic and cytostatic activity of erlangerins from *Commiphora erlangeriana*. Toxicon 41(6):723–727