

Phytochemical and Ethnopharmacological Review of Aegle Marmelos

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Abstract

Aegle marmelos (*AM*) is a fruit-bearing tree native to the Indian subcontinent. It holds a significant place in traditional medicine systems and cultural practices of the region. The aim of the study on *AM* phytochemical and pharmacological investigation of the bioactive compounds present in the plant and to elucidate their potential pharmacological activities. The goal of this research is to better understand ancient medicine and its possible uses in contemporary healthcare. A multidisciplinary approach combining botanical, phytochemical, and pharmacological approaches is required to understand *AM*. The results of a pharmacological and phytochemical study on the *AM* would provide valuable insights into its potential health benefits and the bioactive compounds responsible for those effects. In summary, *AM* is a plant with significant potential for promoting health and well-being, based on both traditional wisdom and emerging scientific knowledge. Its wide range of bioactive compounds makes it an intriguing subject for further research and exploration into its therapeutic applications.

Keywords: Aegle marmelos, Phytoconstituents, Medicinal Property, Pharmacology

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How to Cite This Article: Sahu MK, Tiwari SP. Phytochemical and Ethnopharmacological Review of Aegle Marmelos. Bull Pioneer Res Med Clin Sci. 2024;3(2):29-47.

Introduction

Aegle marmelos (*AM*) is an important medicinal tree in India, commonly known as Bael fruits, Bel, Indian Bael, Bengal Quince, Belan in English and Shivadruma in Sanskrit, Bel or Bael in Hindi [1]. Fruits are green, hard, and smooth woody shells, that belong to the family Rutaceae. Geographically occurring as wild throughout Berma and cultivated at the Sub-Himalayan tract all over India, particularly Central as well as Southern India [2, 3]. This particular variety of tree, which is around 12 metres tall, sheds its leaves every autumn. The Hindu faith holds significant mythological value for the Leaf of the *AM* tree, often referred to as Tripatra, which is crucial for the Lord Shiva puja. The plant has tough, 8-9 meters in height,

aromatic leaves, and round-shaped fruit 5-10 cm in diameter and mucilaginous in taste. Fruits are collected in April–May [4, 5]. Each parts of this tree are used and can be utilized in various fields [6]. *AM* is a high source of different phytochemicals i.e. carotenoids, terpenoids, alkaloids, flavonoids, amino acids, tannins, organic acids fatty acids, etc [7]. The formulation of *AM* is very well-known in history and is used in dysentery and diarrhea. The root is one of the essential parts used in the herbal formulation such as dashmularisht. Leaves contain alkaloids which play a role in reducing blood sugar levels [8]. Seeds are a rich source of oil and possess antibacterial, antiprotozoal along antifungal properties. It works in dose dose-dependent manner it may cause abortion as a result, it should not be used by pregnant woman [9].

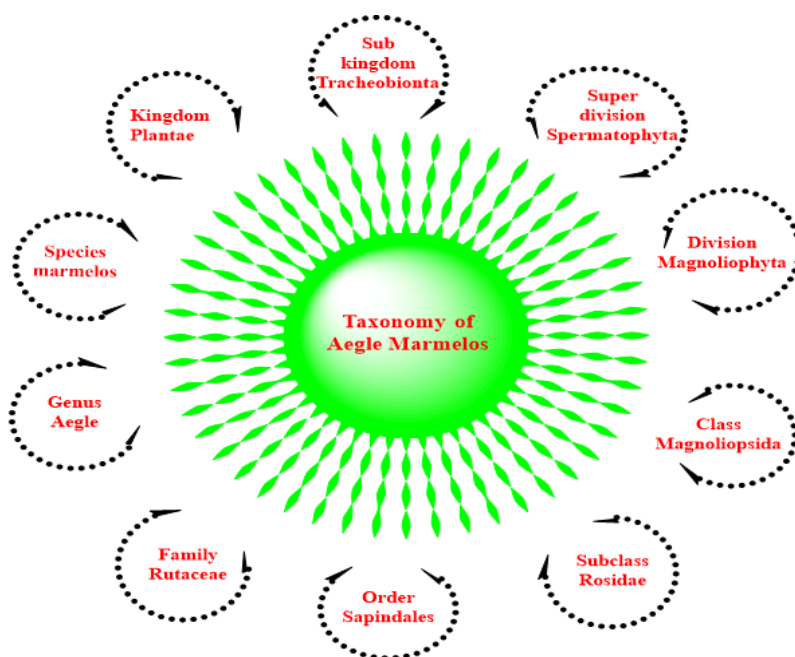


Figure 1. Taxonomical classification of Aegle Marmelos

Phytochemical's

AM, commonly referred to as bael or Bengal quince, Ayurveda, and Traditional Chinese Medicine both use medicinal plants as part of their long-standing regimens [10]. *AM* is well renowned for having a variety of therapeutic benefits and these are attributed to the presence of numerous phytochemicals in its different parts,

including leaves, fruits, and roots. Phytochemicals are naturally occurring bioactive compounds found in plants that often contribute to their potential health benefits [11-13]. The *AM* leaves, roots, and fruits have a variety of chemical constituents Hydro-alcohol is mostly used as a solvent for the extraction of active ingredients from this plant.

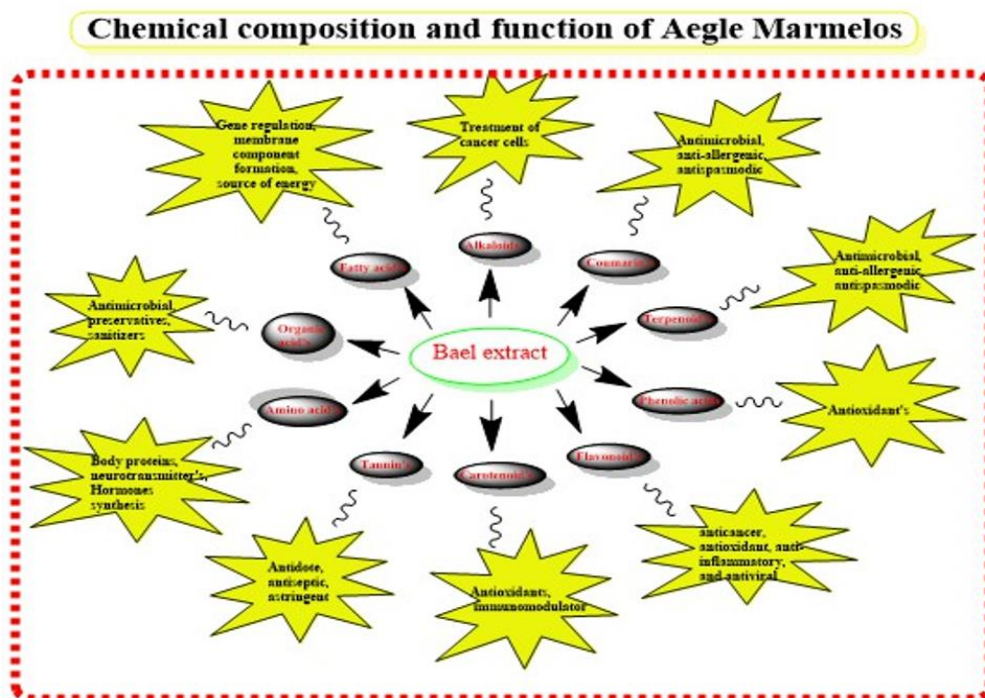
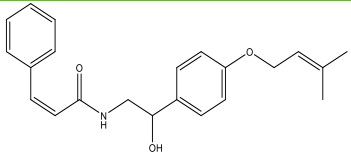
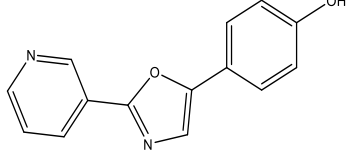
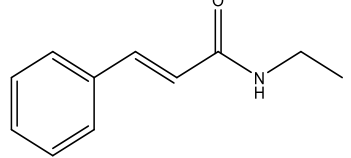
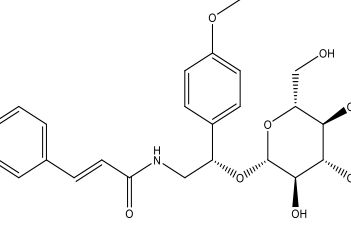
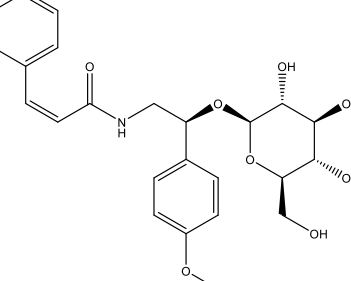
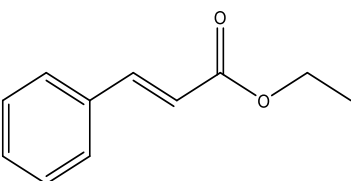
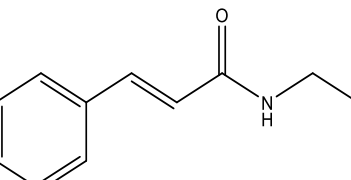
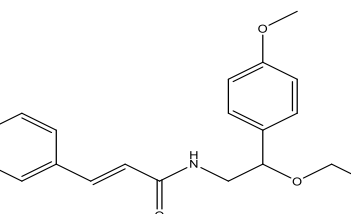


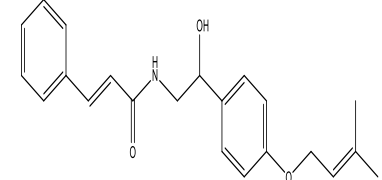
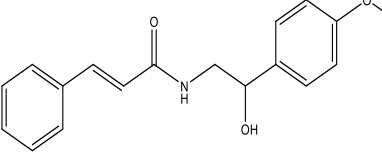
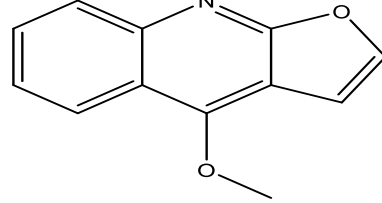
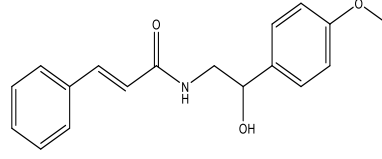
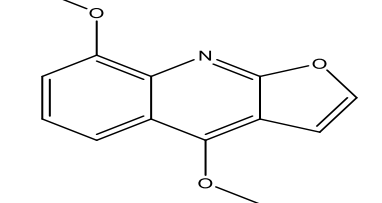

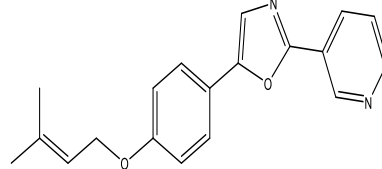
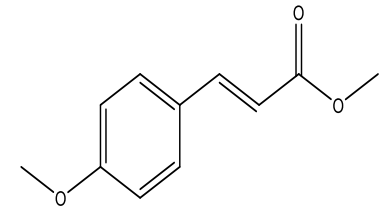
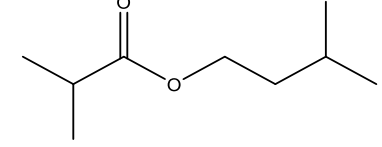
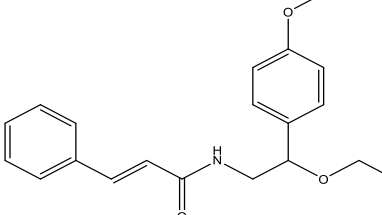
Figure 2. Phytoconstituents and uses of Bael Extract

Literature surveys suggested that *AM* contains a variety of phytochemicals [14]. Alkaloids are used medicinally to treat heart conditions, reduce inflammation, and provide anaesthesia. Leukaemia, renal cell carcinoma, and prostate

cancer were treated with coumarin, terpenoids, and flavonoids. Phenolic as well as amino acids play's role as antioxidants and improve digestive system function [15].

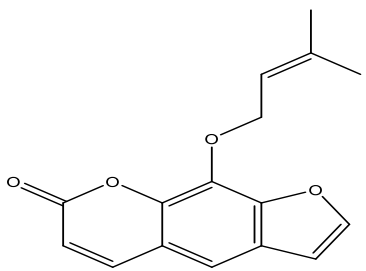
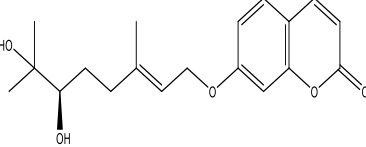
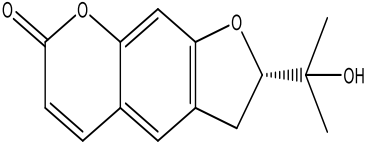
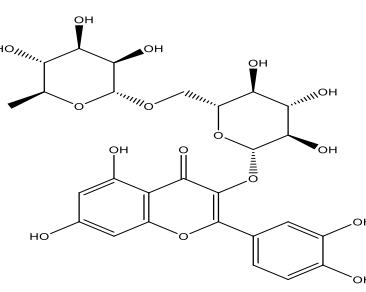
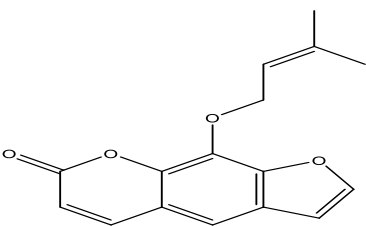
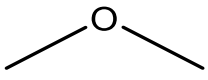
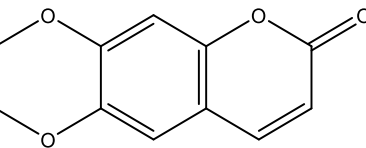
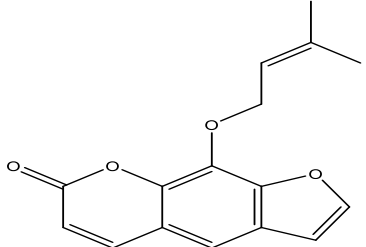
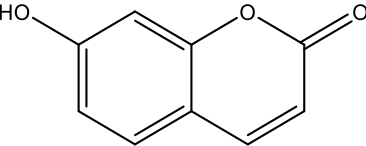
Table 1. Eagle Marmelos chemical composition, separation technique, and medicinal uses

| S. No. | Metabolites | Phytochemicals | IUPAC Name | Molecular structure | Extraction/ Separation Technique | Pharmacology | Reference |
|--------|-------------|-----------------|---|--|--|--|--------------|
| 1. | Alkaloid's | Marmeline | (Z)-N-(2-hydroxy-2-(4-((3-methylbut-2-en-1-yl)oxy)phenyl)ethyl)-3-phenylacrylamide |  | Chromatography Techniques | Cardioprotective, Anaesthetic, anti-inflammatory, Anticancer | [16, 17] |
| | | Halfordino | 4-(2-(pyridine-3-yl)oxazole-5-yl)phenol |  | | | [18-20] |
| | | Ethyl cinnamate | N-ethylcinnamamide |  | | | [21-24] |
| | | Aegelinosides a | N-((S)-2-(4-methoxyphenyl)-2-(((2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)ethyl)cinnamamide |  | | | [25] |
| | | Aegelinosides b | (Z)-N-[(2S)-2-(4-methoxyphenyl)-2-(((2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl)oxyethyl)-3-phenylprop-2-enamide |  | | | [26, 27] |
| | | Ethyl cinnamate | ethyl (E)-3-phenyl prop-2-enoate |  | | | [13, 28, 29] |
| | | Ethyl-cinnamon | N-ethylcinnamamide |  | | | [30, 31] |
| | | Ethanediamine | N-(2-ethoxy-2-(4-methoxyphenyl)ethyl)cinnamamide |  | | | [30] |

| | | | |
|---|--|--|--------------|
| Ethyl Cinnamide | N-(2-hydroxy-2-(4-((3-methylbut-2-en-1-yl)oxy)phenyl)ethyl)cinnamide |  | [31, 32] |
| Aegelin | N-(2-hydroxy-2-(4-methoxyphenyl)ethyl)cinnamide |  | [33-35] |
| Dictamine | 4-methoxyfuro[2,3-b]quinoline |  | [36] |
| Aegelin | N-(2-hydroxy-2-(4-methoxyphenyl)ethyl)cinnamide |  | [37, 38] |
| Fragrine | 4,8-dimethoxyfuro[2,3-b]quinoline |  | [25, 39] |
| Eicosapentaenoic acid | (5E,8E,11E,14E,17E)-icosapentaenoic acid |  | [40, 41] |
| Omethylhalfordinine | 5-(4-((3-methylbut-2-en-1-yl)oxy)phenyl)-2-(pyridin-3-yl)oxazole |  | [42, 43] |
| N-4-methoxystyryl cinnamide | methyl (E)-3-(4-methoxyphenyl)acrylate |  | [26, 44, 45] |
| Oisopentyl halfordinol | isopentyl isobutyrate |  | [46, 47] |
| N-2-ethoxy-2-(4-methoxyphenyl)ethyl cinnamide | N-(2-ethoxy-2-(4-methoxyphenyl)ethyl)cinnamide |  | [45, 48] |

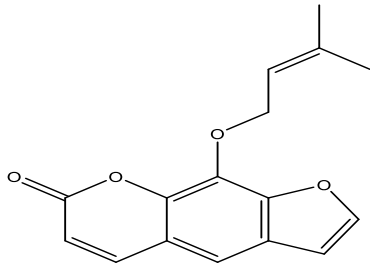
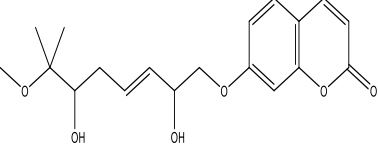
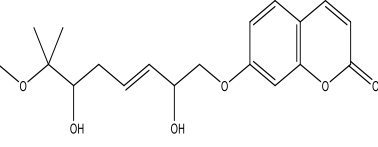
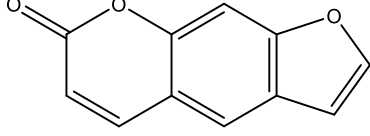
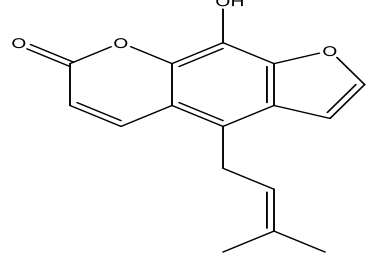
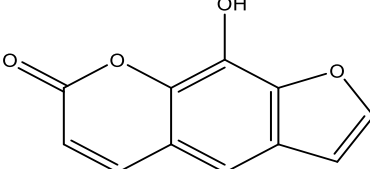
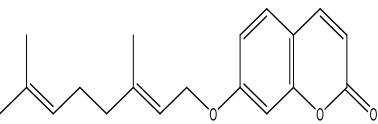
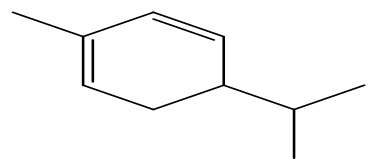
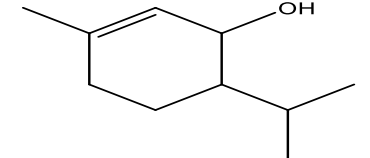
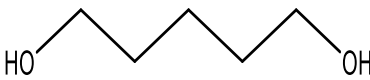
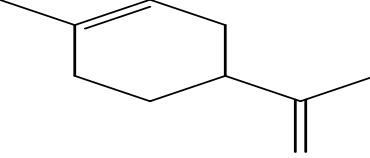
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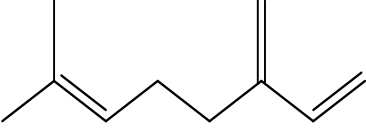
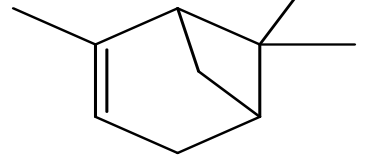
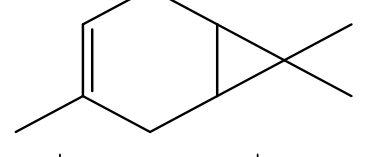
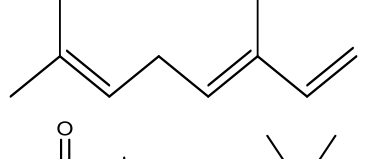
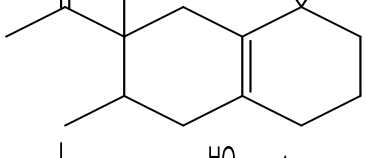
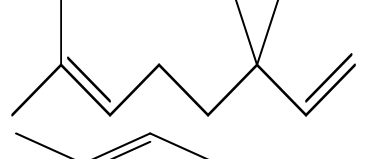
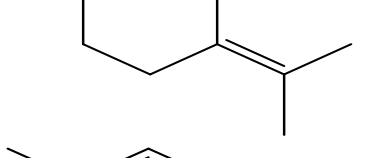
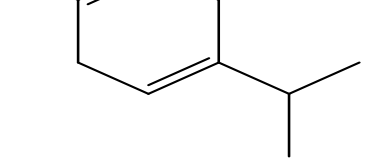
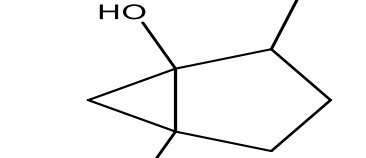
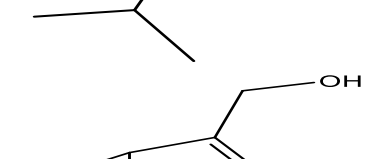
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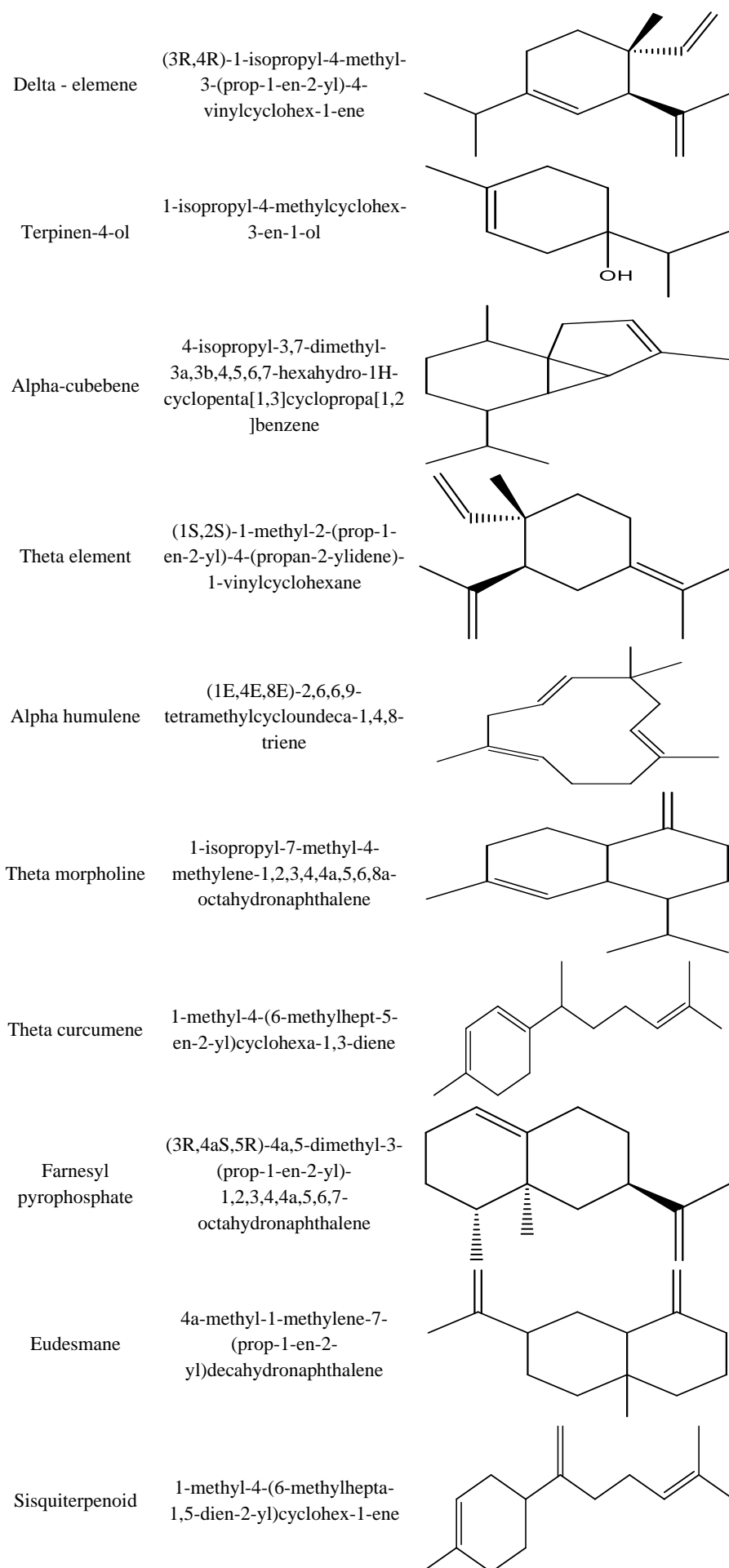
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|---------------|--|--|--------------|
| Marmelosin | 9-((3-methylbut-2-en-1-yl)oxy)-7H-furo[3,2-g]chromen-7-one |  | [33, 49-52] |
| Marmin | (R, E)-7-((6,7-dihydroxy-3,7-dimethyloct-2-en-1-yl)oxy)-2H-chromen-2-one |  | [53-55] |
| 3marmesin | (S)-2-(2-hydroxypropan-2-yl)-2,3-dihydro-7H-furo[3,2-g]chromen-7-one |  | [56-58] |
| Rutacine | 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-(((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(((2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)-4H-chromen-4-one |  | [59, 60] |
| Marmelosin | 9-((3-methylbut-2-en-1-yl)oxy)-7H-furo[3,2-g]chromen-7-one |  | [49, 61, 62] |
| Methyl ether | methoxymethane |  | [63-65] |
| Scoparome | 6,7-dimethoxy-2H-chromen-2-one |  | [66] |
| Imperatorin | 9-((3-methylbut-2-en-1-yl)oxy)-7H-furo[3,2-g]chromen-7-one |  | [67, 68] |
| Umbelliferone | 7-hydroxy-2H-chromen-2-one |  | [69-71] |

Chromatographic separation

Prostate cancer, renal cell carcinoma, and leukemia

| | | | | |
|--------------|-----------------------|---|--|-------------|
| | Marmelide | 9-((3-methylbut-2-en-1-yl)oxy)-7H-furo[3,2-g]chromen-7-one |  | [72, 73] |
| | Mermenol | (E)-7-((2,6-dihydroxy-7-methoxy-7-methyloct-3-en-1-yl)oxy)-2H-chromen-2-one |  | [74] |
| | Scopolentin | (E)-7-((2,6-dihydroxy-7-methoxy-7-methyloct-3-en-1-yl)oxy)-2H-chromen-2-one |  | [75] |
| | Psoralen | 7H-furo[3,2-g]chromen-7-one |  | [76] |
| | Alloimperaterin | 9-hydroxy-4-(3-methylbut-2-en-1-yl)-7H-furo[3,2-g]chromen-7-one |  | [77] |
| | Zanthotaxol | 9-hydroxy-7H-furo[3,2-g]chromen-7-one |  | [78] |
| | Epoxyauraptan | (E)-7-((3,7-dimethylocta-2,6-dien-1-yl)oxy)-2H-chromen-2-one |  | [79] |
| 3. Terpenoid | Alpha phellandrene | 5-isopropyl-2-methylcyclohexa-1,3-diene |  | [80] |
| | 3-Carvomenthenol | 6-isopropyl-3-methylcyclohex-2-en-1-ol |  | |
| | Pentamethylene glycol | pentane-1,5-diol |  | |
| | Dipentene | 1-methyl-4-(prop-1-en-2-yl)cyclohex-1-ene |  | |
| | | | Hydrodistillation, steam distillation, and solvent extraction | |
| | | | Immune modulator, antifungal, antiviral, antiparasitic, antispasmodic, antihyperglycemic | [31, 81-83] |

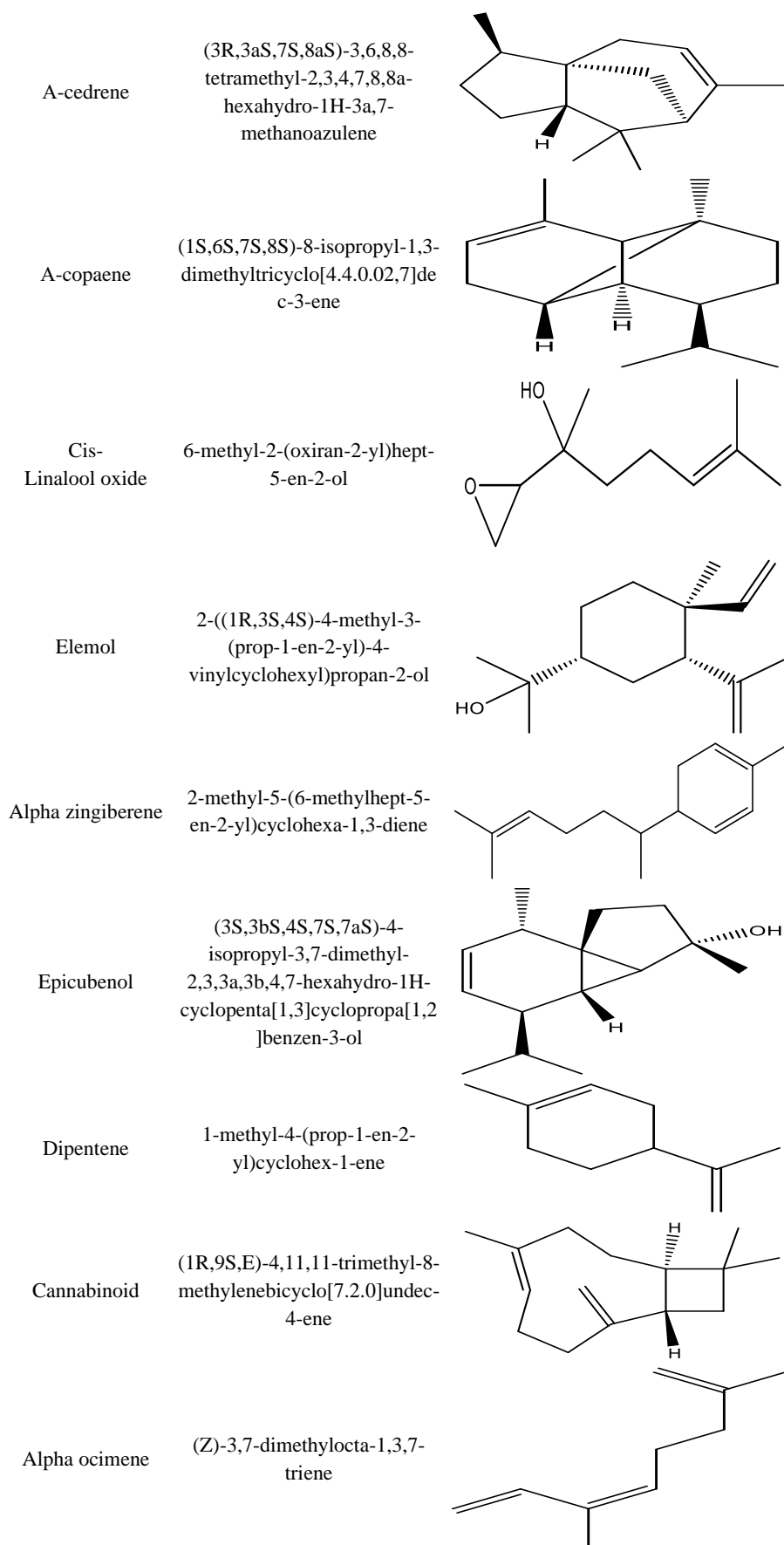
| | | | |
|------------------|---|--|------|
| Ocimene | 7-methyl-3-methyleneocta-1,6-diene |  | |
| Australene | 2,6,6-trimethylbicyclo[3.1.1]hept-2-ene |  | [32] |
| Delta-3-Carene | 3,7,7-trimethylbicyclo[4.1.0]hept-3-ene |  | [30] |
| B-ocimene | (E)-3,7-dimethylocta-1,3,6-triene |  | [84] |
| Boisvelon | 1-(2,3,8,8-tetramethyl-1,2,3,4,5,6,7,8-octahydronaphthalen-2-yl)ethan-1-one |  | [39] |
| Licareol | 3,7-dimethylocta-1,6-dien-3-ol |  | [85] |
| Isoterpinene | 1-methyl-4-(propan-2-ylidene)cyclohex-1-ene |  | |
| Moslene | 1-isopropyl-4-methylcyclohexa-1,4-diene |  | |
| Butanoic acid | 5-isopropyl-2-methylbicyclo[3.1.0]hexan-1-ol |  | |
| Thujen-3en-10-ol | (5-isopropylbicyclo[3.1.0]hex-2-en-2-yl)methanol |  | [32] |



| | | |
|-----------------------------|---|--|
| Levomenol | (S)-4-methyl-1-((S)-6-methylhept-5-en-2-yl)cyclohex-3-en-1-ol | |
| Theta cardinene | 1-isopropyl-7-methyl-4-methylene-1,2,3,4,4a,5,6,8a-octahydronaphthalene | |
| Alpha terphenyl isobutyrate | 2-(4-methylcyclohex-3-en-1-yl)propane-2-yl isobutyrate | |
| Cis, Trans Farnesol | (2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-ol | |
| 2-cis, 6-trans-Farnesol | (2Z,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-ol | |
| 3z-hexenol | (Z)-hex-1-en-1-ol | |
| Ethyl hexoic acid | ethyl hexanoate | |
| Methyl Perillate | methyl (2E,4E)-5-(benzo[d][1,3]dioxol-5-yl)penta-2,4-dienoate | |
| Alpha-Cardinol | (1R,4S,4aR,8aR)-4-isopropyl-1,6-dimethyl-1,2,3,4,4a,7,8,8a-octahydronaphthalen-1-ol | |
| Eucalyptol | 1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane | |
| Limonene oxide | (1S,4R)-1-methyl-4-(prop-1-en-2-yl)-7-oxabicyclo[4.1.0]heptane | |

[31]

[30]



[31]

| | | | | | |
|----|------------------|--|---|-----------------------|----------------|
| | Epicubenol | (1S,4R,4aR,8aR)-1-isopropyl-4,7-dimethyl-1,3,4,5,6,8a-hexahydronaphthalen-4a(2H)-ol | | | |
| | Alpha humulene | (1E,4E,8E)-2,6,6,9-tetramethylcycloundeca-1,4,8-triene | | | |
| | Beta myrcene | 7-methyl-3-methyleneocta-1,6-diene | | | |
| | Alpha copaene | (1S,6S,7S,8S)-8-isopropyl-1,3-dimethyltricyclo[4.4.0.0.2,7]dec-3-ene | | | |
| | Chlorogenic acid | (1S,3R,4R,5R)-3-(((E)-3-(3,4-dihydroxyphenyl)acryloyl)oxy)-1,4,5-trihydroxycyclohexane-1-carboxylic acid | | | |
| | Rutaretin | (S)-9-hydroxy-2-(2-hydroxypropan-2-yl)-2,3-dihydro-7H-furo[3,2-g]chromen-7-one | | | |
| 4. | Phenolic acid' s | Gallic acid | 3,4,5-trihydroxybenzoic acid | | |
| | | Vanillic acid | 4-hydroxy-3-methoxybenzoic acid | | |
| | | Caffeic acid | (E)-3-(3,4-dihydroxyphenyl)acrylic acid | | |
| | | Gentisic acid | 2,5-dihydroxybenzoic acid | | |
| | | | | Column Chromatography | Antioxidant' s |

| | | | | |
|----|--------------|-------------------|--|--|
| 5. | Flavonoid's | Syringic acid | 4-hydroxy-3,5-dimethoxybenzoic acid | |
| | | Procatechuic acid | 3,4-dihydroxybenzoic acid | |
| | | Ferulic acid | (E)-3-(4-hydroxy-3-methoxyphenyl)acrylic acid | |
| | | P- coumaric Acid | (E)-3-(4-hydroxyphenyl)acrylic acid | |
| | | Quercetin | 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one | |
| | | Rutin | 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-(((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(((2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)-4H-chromen-4-one | |
| 6. | Carotenoid's | Catechin | (2R,3S)-2-(3,4-dihydroxyphenyl)chromane-3,5,7-triol | |
| | | Flavan-3-ol | 2-phenylchroman-3-ol | |
| | | Skimminianine | 2-phenylchroman-3-ol | |

Chromatographic techniques

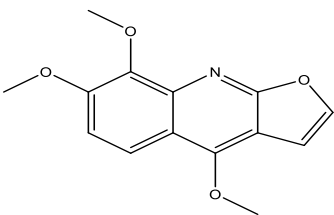
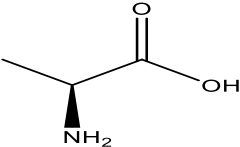
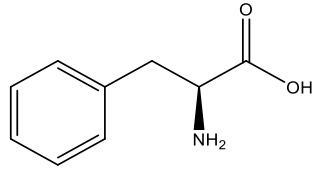
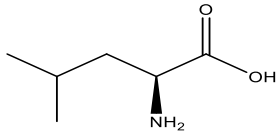
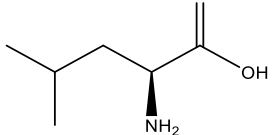
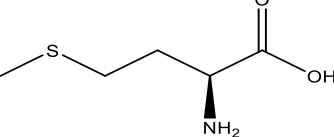
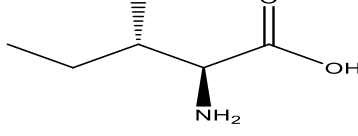
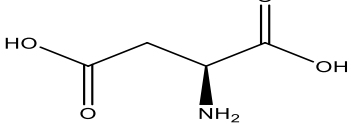
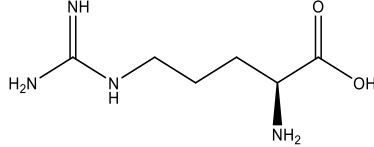
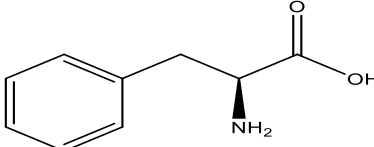
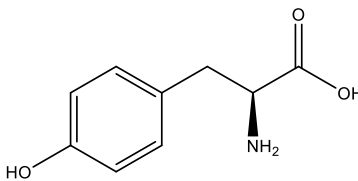
Chromatography

anticancer, antioxidant, anti-inflammatory, and antiviral properties

Antioxidants, immunomodulator

[10]

[18]

| | | | | | | |
|----|--------------|----------------------------------|--|--|---|---|
| 7. | Tannin's | 4, 7, 8-trimethoxyfuro-quinoline | 4,7,8-trimethoxyfuro[2,3-b]quinoline |  | Extraction technique | Antidote, antiseptic and astringent |
| | | Alanine | (2S)-2-aminopropanoic acid |  | | |
| | | Phenyl alanine | (2S)-2-amino-3-phenylpropanoic acid |  | | |
| | | Tyrosine | L-tyrosine |  | | |
| | | Leucine | (2S)-2-amino-4-methylpentanoic acid |  | | |
| | | Methionine | (2S)-2-amino-4-methylsulfanylbutanoic acid |  | | |
| | | Isoleucine | (2S,3S)-2-amino-3-methylpentanoic acid |  | | |
| 8. | Amino acid's | Aspartic acid | (2S)-2-aminobutanedioic acid |  | Ion exchange, metal affinity, and gel filtration chromatography | Body proteins, neurotransmitter's, and Hormones synthesis |
| | | Arginine | (S) - 2-Amino - 5-guanidinopentanoic acid |  | | |
| | | Phenyl alanine | (2S) - 2 - amino - 3-phenylpropanoic acid |  | | |
| | | Tyrosine | (2S)-2-amino-3-(4-hydroxyphenyl)propanoic acid |  | | |

[14]

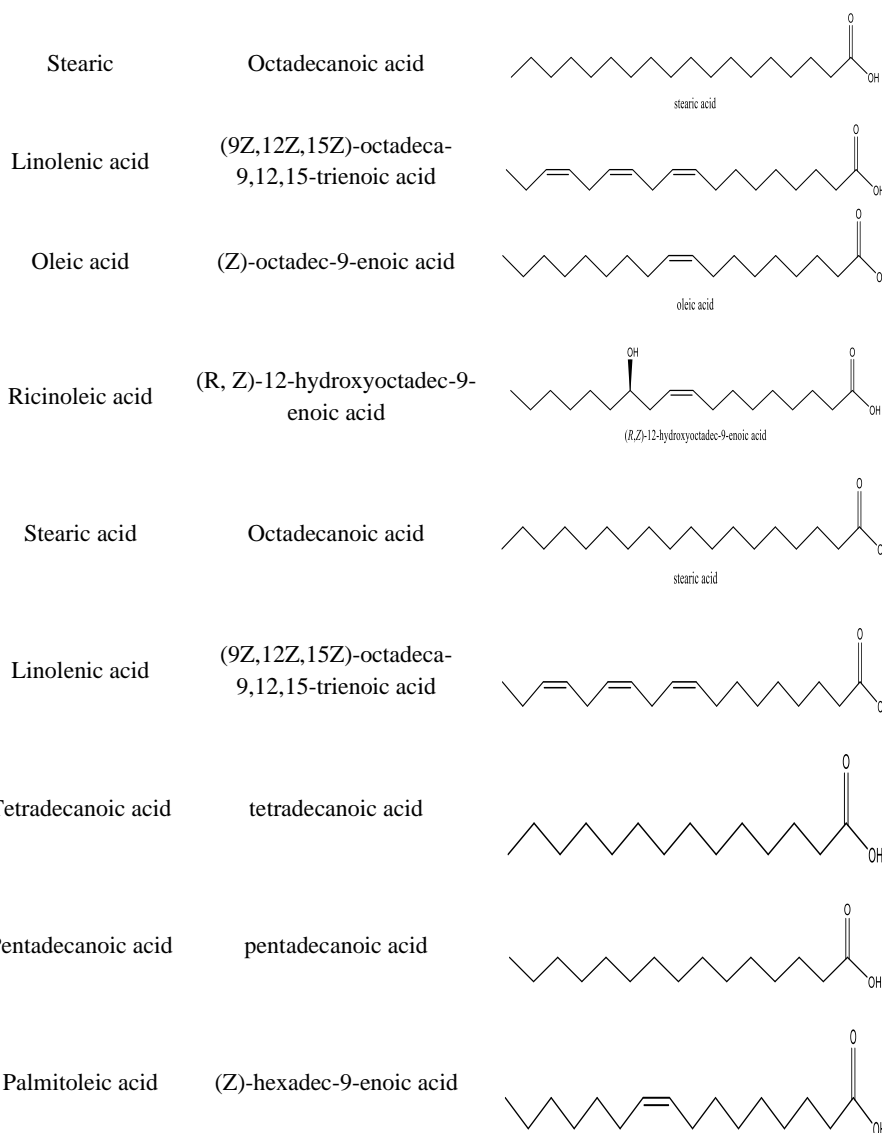
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|-----|----------------|---------------|---|--|------|
| 9. | Organic acid's | Leucine | (S)-2-amino-5- ((diaminomethylene)amino)pe ntanoic acid | | [25] |
| | | Methionine | (2S)-2-amino-4- methylsulfanylbutanoic acid | | |
| | | Isoleucine | (2S,3S)-2-amino-3- methylpentanoic acid | | |
| | | Aspartic acid | (2S)-2-aminobutanedioic acid | | |
| | | Arginine | (S)-2-amino-5- ((diaminomethylene)amino)pe ntanoic acid | | |
| | | Alanine | (2S)-2-aminopropanoic acid | | |
| | | Oxalic acid | Oxalic acid | | |
| | | Malic acid | 2-hydroxysuccinic acid | | |
| | | Tartaric acid | (2R,3R)-2,3-dihydroxysuccinic acid | | |
| 10. | Fatty acid's | Linoleic | (9Z,12Z)-octadeca-9,12- dienoic acid | | [25] |
| | | Palmitic | Hexadecanoic acid | | |

anion exchange, ion exclusion, and reversed-phase
high-performance liquid chromatography

Antimicrobials, preservatives, and sanitizers

Low-temperature
crystallization, distillation,
and precipitation techniques

Gene regulation, membrane
component formation, and
source of energy



Medicinal and pharmacological properties

Anticancer activity

Studies suggested that certain compounds found in bael, including alkaloids and essential oils, may exhibit cytotoxic effects on cancer cells [19]. AM extract shows significant inhibition on MCF 7 and MDAMB 231 breast cancer cell line [6]. These compounds could interfere with the growth and division of cancer cells, leading to their destruction [19].

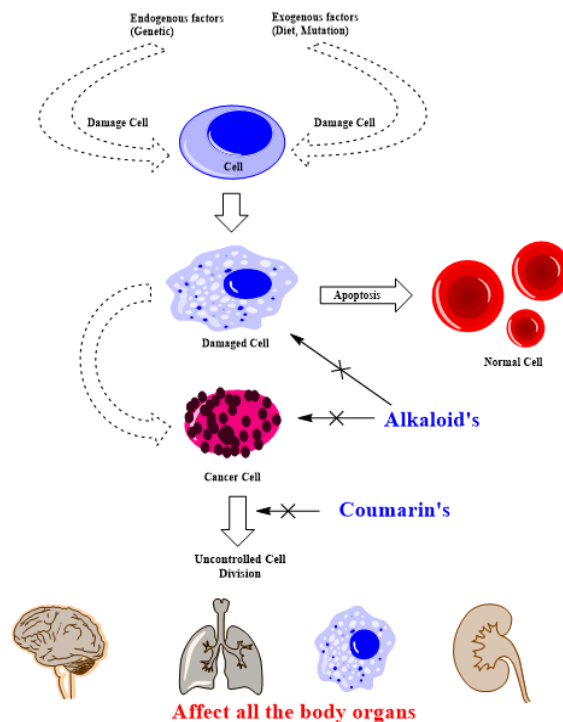


Figure 3. Anticancer effect of AM

Antidiabetic activity

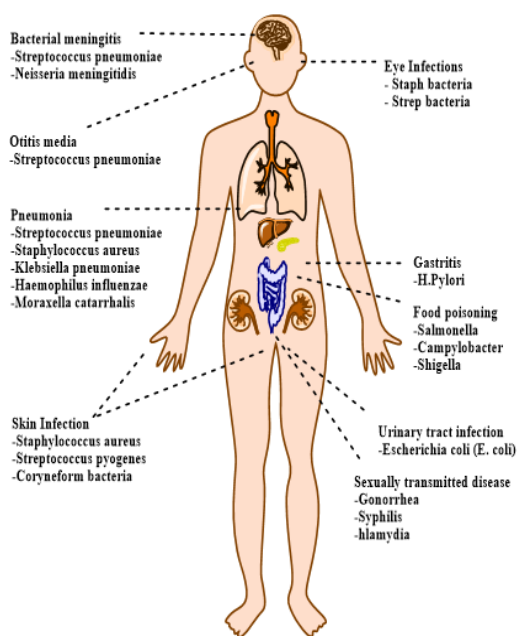
Diabetes mellitus is a common metabolic disorder [72, 86]. AM hydro-alcoholic extract helps to reduce the blood sugar level as well as significantly increase the blood insulin and liver glycogen in diabetic rats [10, 42].

Anti-ulcer activity

Currently, due to lifestyle gastric disorders are common, Researchers reported that the methanolic extract of bael is highly effective for reducing gastrointestinal ulcers [35, 47].

Antimicrobial activity

The antibacterial activity of the different AM extracts was tested quinine compound was identified as possessing good antibacterial activity [66]. Researchers found that extract is highly effective as compared to other allopathic preparations against gram-positive and negative bacteria [18, 55].



Schematic diagram of bacterial infection

Figure 4. Antibacterial effect of AM

Antioxidant activity

Oxidative stress is induced due to physical, chemical, environmental as well as biological factors which cause the generation of free radicals [51]. AM phytoconstituents play a crucial role in free radical scavenging, these alteration returns the free radical to normal levels which reveals the antioxidant activity of bael extract [67, 83].

Anti-hyperlipidemic activity

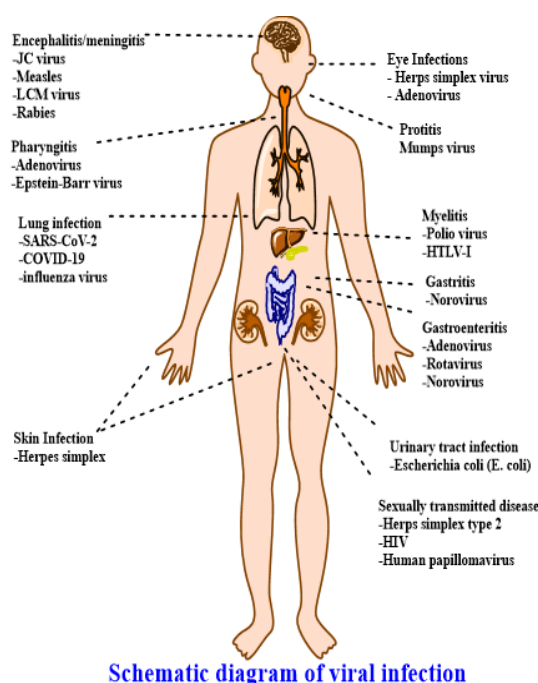
Literature surveys reveal that bael extract induces the utilization of elevated fatty acids and their types [74]. As a result, lower levels of fatty acids were formed which is an important channel for consumption of higher glucose molecules [58].

Radioprotective action

In recent times radiotherapy has been one of the important causes of cancer because of its free radical formation-inducing property. AM extract was reported for the free radical scavenging of radiation-induced free radicals [73]. The radioprotective activity was studied in Swiss albino rats that were given a lot of intraperitoneal single doses of the extract [74].

Antiviral activity

The ability of different varieties of fungi to grow is tested by the separated volatile oil from AM [72]. The essential oil fully stopped all fungi from generating spores at a dosage of 0.05%. Around 75% and 90% of the fungus are significantly suppressed at 0.03% - 0.04%, respectively [66].



Schematic diagram of viral infection

Figure 5. Antiviral of AM

Conclusion

The present study suggested that the therapeutic potential of AM and the phytoconstituents may be utilized to develop unique formulations for the management, mitigation as well as prevention of cancer, diabetes mellitus, and other microbial diseases [47]. Numerous ethnobotanical uses of AM have been documented in the past. Unfortunately, the majority of substances still need to be carefully examined to look into new lead molecules or pharmacophores. A few bioactive compounds' processes have also so far been identified. To determine the pathophysiology as well as the pharmacology of various phytochemicals with the efficacy of AM pharmacological properties, extensive research is required [1].

Acknowledgments: The principal of the MATS School of Pharmacy in Raipur, Dr. Amit Nayak, is acknowledged by one of the authors for his consistent support and inspiration.

Conflict of interest: None

Financial support: None

Ethics statement: None

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