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← Adınızı soyadınızı giriniz

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← Tez Sınavının yapılacağı yılı yazınız

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**EVALUATION OF BIOLOGICAL ACTIVITIES OF MELIA
AZEDARACH SPECIES AND ITS IMPORTANCE IN
PHYTOTHERAPY**

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DEDICATION

The thesis dedicated to my dearest family .



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LIST OF SYMBOLS / ABBREVIATIONS

μ l : Microliter

A. indica: *Azadirachta indica*

AChE: Acetyl cholinesterase

AD: Alzheimer disease

ALP: Alkaline phosphatase

ALT: Alanine transaminase

AST: Aspartate transaminase

BC: Before Christ

BChE: Butyryl cholinesterase

cm: Centimeter

DPPH: 2, 2- diphenyl-2-picrylhydrazyl

DSÖ: Dünya Sağlık Örgütü

E. coli: *Escherichia coli*

E. vittella: *Earias vittella*

ELISA: Enzyme-linked immunoassay

h: Hour

IFN- γ : Interferon-gamma

kg: Kilogram

LC₅₀: Lethal Concentration 50

LDH: Lactate dehydrogenase

M. azedarach: *Melia azedarach*

m: Meter

max: Maximum

mg: Milligram

ml: Milliliter

ml: Milliliter

mm: Millimeter

sp: Species

TCM: Traditional Chinese Medicine

TNF- α : Tumor necrosis factor alpha

WHO: World Health Organization



GENİŞLETİLMİŞ ÖZET

Eswiei, Khawla (2023). *Melia azedarach* türünü biyolojik aktivitelerinin değerlendirilmesi ve fitoterapideki önemi. İstanbul Üniversitesi Sağlık Bilimleri Enstitüsü, Eczacılık Fakültesi, Farmakognozi Anabilim Dalı. Yüksek Lisans Tezi. İstanbul.

Amaç: Bu çalışmanın amacı, *Melia azedarach*'ın biyolojik aktiviteleri ve kimyasal bileşimi ile ilgili güncel literatürleri kapsamlı bir şekilde gözden geçirerek, fitoterapideki mevcut kullanımını incelemek ve potansiyelini belirlemektir.

Kapsam: Bu çalışma *Melia azedarach*'ın kimyasal bileşimini, biyolojik aktivitesini, farmakolojik özelliklerini, etki mekanizmalarını ve fitoterapideki terapötik uygulamalarını inceleyen çalışmaları kapsamaktadır.

Yöntem: Bu çalışma Google akademik, PubMed, Science Direct, Thyme, Wiley, Web of Science, Springer ve Taylor and Francis veri tabanları kullanılarak *Melia azedarach*, chemical composition, biological activities, phytotherapy anahtar kelimeleri ile yapılan taramaların sonuçlarında bulunan literatürlerdeki bilgilerin derlenmesiyle hazırlanmıştır.

Bulgular: Bu literatür tarama sonuçlarında yaklaşık 350 yayına ulaşılmış ve bunlar içerisinden ilgili 55 yayın tezin yazımında kullanılmıştır. Bu yayınlar *Melia azedarach* türünün kimyasal bileşimi ve biyolojik aktiviteleri ile ilgili yapılan çalışmalardan oluşmaktadır.

Tartışma ve Sonuç: Geleneksel tıbbın temelini oluşturan tıbbi bitkiler, gelişmemiş ya da gelişmekte olan ülkelerde yaşayan 3.3 milyardan fazla insanın düzenli olarak tedavide kullandığı ürünlerdir. Ayrıca, Dünya Sağlık Örgütü (DSÖ), dünya nüfusunun %80'den fazlasının ana sağlık ihtiyaçları için hala geleneksel tıba güvendiğini tahmin etmektedir. DSÖ, sağlık sisteminde geleneksel tıbbın önemini vurgulamış ve bitkisel ilaçlar için stratejiler, kılavuzlar ve standartlar oluşturmuştur. Tıbbi bitkiler sadece geleneksel kullanım sınırlı değildir, aynı zamanda modern ilaçların geliştirilmesinde zengin bir içerik kaynağı olarak da değerlendirilmektedir. Kimyasal olarak sentezlenen ilaçlara karşı olumsuz etkilerin ve mikrobiyal direncin gelişmesi nedeniyle, bilim insanları etnofarmakognoziye yönelmiştir. Tıbbi bitkiler, farklı kısımlarında bulunan biyoaktif bileşiklerden kaynaklanan doğal iyileştirme özellikleri sayesinde fitoterapide kritik bir rol oynar. Bu bileşikler, anti-inflamatuar, antimikrobiyal, antioksidan ve immünomodülatör özelliklere ve terapötik etkilere sahiptir. Bu aktiviteler, tıbbi bitkilerin genellikle sinerjik olarak etkileşen aktif bileşiklerin kombinasyonunu içermelerinden kaynaklanır. Ancak, bitkisel çözümlerin birbirleriyle veya ilaçlarla etkileşimleri olabilir. Bu nedenle uzman görüşü ve takibi ile kullanılmaları gerekmektedir.

Bu tür bitkilerden biri olan *Melia azedarach* L. (Chinaberry), Meliaceae familyasına ait, yaygın olarak "Çin ağacı," "boncuk ağacı", "Hint Kirazı", "Hint Lalesi" ve "Pers çitlembiği" olarak bilinen, Güneydoğu Asya (Hindistan, Pakistan, Çin, Burma, Bangladeş) ve Avustralya'ya özgü bir ağaçtır. Meliaceae familyasında genellikle ağaçlar veya çalılar, nadiren alt çalılar olur, dünya çapında yayılış gösteren yaklaşık 50 cins ve 550'den fazla tür içeren çiçekli bir bitki grubudur. *Melia azedarach* bitkisi, büyük ve bileşik yapraklarıyla dikkat çeker ve boyları 15 metreye kadar ulaşabilir. Bitki, yaz aylarında çiçek açar ve çiçekleri salkım şeklinde dizilir, sonrasında boncukları andıran sarı meyvelere dönüşür. Bu nedenle Türkçede "tesbih ağacı" olarak isimlendirilmiştir. Zorlu çevresel koşullara karşı yüksek toleransı olması, büyüme hızı ve verimli tohum üretimi sayesinde süs bitkisi olarak sıcak-ılıman ve tropikal bölgelerde (Hindistan, Pakistan, Nepal, Sri Lanka, Doğu Timor, Endonezya, Lübnan, Filistin, Suriye, Tunus, Cezayir, Kıbrıs, Yunanistan, Arjantin, Çin, Uganda, Kenya, Brezilya, Avustralya, Güney Fransa, Kuzey İtalya, Hırvatistan ve Portekiz) yetiştirilmektedir. Bu tür, yüksek kaliteli kereste ürettiği için ekonomik açıdan ilgi çekicidir ve sıklıkla mobilya, tarım araçları, botlar, araçlar, kontrplak, oyuncaklar ve müzik aletleri yapmak için kullanılır; ayrıca zorlu iklim ve toprak koşullarına dayanabilme özelliği nedeniyle süs ağacı olarak yaygın bir şekilde kullanılır. Ayrıca, bu tıbbi bitkinin farklı kısımlarının özleri farmakolojik ve toksikolojik özelliklere sahiptir.

Bu bitkinin terapötik kullanımları Ayurveda, Siddha ve Yunani Tıbbi Sistemlerinde belgelenmiştir. Bu sistemlere göre kök kabuğu ve meyve cilt kurutucu, tonik, müshil, yumuşatıcı ve antihelmintik özelliklere sahiptir. Gövde kabuğu acı, tonik, cilt kurutucu, sara karşıtı ve solucan düşürücüdür. Yapraklar antiinflamatuvar ve antihelmintik etkiye sahiptir. Tohum yağı uyarıcı, böcek öldürücü ve antiseptiktir.

M. azedarach'ın çeşitli kısımları, gövde kabukları, yaprakları, meyveleri ve tohumları, mide rahatsızlığı, kusma, kanlı ishal, cüzzam, vitiligo, böbrek taşı, bağırsak tıkanıklığı gibi çeşitli hastalıkların tedavisinde halk arasında uzun yıllar kullanılmıştır.

Bitkinin yaprakları, meyveleri, kabuk, tohum ve kökleri ile yapılan araştırmalarla bu drogların antifungal, antimalaryal, antibakteriyel, hepatoprotektif, antioksidan, anti-fertilite, anthelmintik, antipiretik ve sitotoksik aktiviteler gösterdiği belirlenmiştir.

Bitkinin bu biyolojik etkinlikleri içeriğindeki yüksek oranda bulunan limonoid bileşiklerinin (azedaralid, nimbolinin, nimbolidin, sendanin, sendenal, melianon, azadiraktin ve gedunin) yanı sıra diğer fenolik asitler, terpenoidler (diterpenoidler, triterpenoidler, tetranortriterpenoidler, seskiterpenoidler), fenolik bileşikler, flavonoidler (kaempferol, kaempferol-3-O-β-rutinoside, rutin, apigenin-5-O-β-D-galaktopiranosid), ligninler, antrakınonlar, poliketidler (amoorastatin ve amorastaton), hidrosikumarin türevleri, steroidler (6-β-Hidroksi-4-stigmasten-3-on, β-Sitosterol-β-D-glikozit, kampesterol, 4-Stigmastanen-3-1,4-kampesten-3-on-β-sitosterol, dokosterol, stigmasterol, β-sitosterol) ve alkaloidlerin varlığına dayandırılmaktadır. Örneğin alkaloidler, bitkinin iç kabuğunda bulunur ve genellikle antihelmintik etkiden

sorumludur. Ancak, bu bileşiklerin kompozisyonu bitkinin coğrafi kökenine bağlı olarak değişebilir. Günümüze kadar yapılan çalışmalar bitkiden izole edilen ve tanımlanan bileşenleri özetlemektedir. Bu bileşenler arasında kersetin, kaempferol, rutin, mirisetin, ve izoramnetin (flavonoidler), kampesterol, stigmasterol (fitosteroller), fitol (diterpen), heptadekan, β -sitosterol, heksadekanoik asit, tokoferol, β -karoten, 1-eikosanol (triterpen), terpen alkol ve skualen bulunmaktadır. Ayrıca, β -D-glukopiranoz, daükosterol, liminoid glikozit, melianol, meliakarpin, meliasin, (\pm) pinosinonol, hidroksil-3-metoksisinnamaldehit ve azadiraktin-A ve azadiraktin-B gibi terpenoidler de yer almaktadır.

M. azedarach, geçmişten günümüze geleneksel tıbbi kullanımları olan çok yönlü bir bitkidir. Modern araştırmalar, bitkinin farklı kısımlarında çeşitli biyoaktif bileşenlerin varlığını ortaya koymuş ve çeşitli biyolojik aktivitelerini göstermiştir. *M. azedarach* yaprak ekstreleri antiviral ve antifertilite aktivitelerine sahiptir, meyve ekstresi ise ovisidal, larvasidal ve antioksidan aktiviteye sahiptir. Sulu ekstresi indirgeyici potansiyele sahiptir. Protein tirozin fosfataz enziminin etkilerini inhibe ederek antidiyabetik potansiyele sahip olduğu rapor edilmiştir. Bitkinin metanolik ham ekstresinden gümüş nanopartiküllerin yeşil sentezi yapılmış ve antimikrobiyal, antibakteriyel, antidiyabetik ve yara iyileştirici aktiviteler saptanmıştır. *M. azedarach*'ın metanolik ekstresi üzerinde MCF-7 hücre hatlarında antikanser aktivitesi bildirilmiştir.

Özellikle *Melia azedarach* kabuğunda bulunan 2, 3-Dihidrobenzofuran ve 5-hidroksipipekolik asit gibi bileşiklerin diyabetik retinopati, artrit ve trombosit agregasyonunu önleme gibi potansiyele sahip olduğu gözlemlenmiştir. Ayrıca, yine bu türden elde edilen pirazol-5(2H)-on adlı bir flavonoidin de antiinflamatuvar, ateş düşürücü ve analjezik etkilere sahip olduğu saptanmıştır.

Melia azedarach yaprakları, kabuğu ve çiçeklerinin memelilere zehirli olduğu bildirilmiştir. Zehirlenmeler çoğunlukla domuzlar (en yaygın etkilenenler), sığır, koyun, keçi, kümes hayvanları, köpekler ve hatta insanlarda görülmüştür. Bu zehirlenmelerin çoğu *M. azedarach*'ın meyvelerinin tüketilmesinden kaynaklanmaktadır. Bu nedenle bitkinin kısımlarının ve/veya ürünlerinin kullanımı memeliler de dahil olmak üzere birçok organizmalar için zehirli olabileceğinden çok dikkatle kullanılmalıdır. Toksik bileşikler mide ve bağırsak tahrişine ve karaciğer ile böbreklerde dejenerasyona neden olabilir.

Bu bitkiden elde edilen fenolikler ve fitosterollerin kozmetik ve ilaç uygulamaları için önemli olduğu çalışmalarla belirtilmektedir. Bununla birlikte, kompleks fenolik bileşiminin anlaşılması için daha fazla çalışmaya ihtiyaç vardır ve içeriğindeki kimyasal bileşiklerin biyolojik aktivite üzerindeki etkilerini aydınlatmak için ileri çalışmalara ihtiyaç vardır.

Bu çalışmanın bulguları, *M. azedarach*'ın fitoterapideki terapötik potansiyelini vurgulamaktadır. *Melia azedarach*'ın fitoterapideki öneminin nedenlerinin başında,

çeşitli bakteri, mantar ve parazit türlerine karşı gösterdiği antimikrobiyal aktivite gelmektedir. Antimikrobiyal özelliklerinin yanı sıra, *Melia azedarach*'ın antioksidan ve anti-inflamatuar etkinliklerinin olması da fitoterapideki yeri açısından önemlidir. *Melia azedarach*'ın en önemli biyolojik aktivitelerden biri olan antibakteriyel etkinliğiyle ilgili birçok çalışma yapılmıştır. Bu çalışmalar, bitkinin çeşitli bakteri suşlarının büyümesini engelleme yeteneğine sahip olduğunu göstermiştir. Bu aktivite, bitkinin doğal bir antimikrobiyal ajan olarak potansiyelini gösteren “azadiraktin”, “gedunin” ve “meliakarpin” gibi limonoidlere bağlanmaktadır. Antibiyotiklere karşı direncin artması alternatif tedavi seçeneklerinin araştırılmasını gerektirdiğinden, bu bulgu fitoterapi alanında büyük önem taşımaktadır.

Ayrıca, *Melia azedarach* dikkate değer bir antifungal aktivite sergilemiştir. Araştırmalar, mantar enfeksiyonlarının tedavisinde potansiyel kullanımını vurgulayarak, mantar patojenleri *Aspergillus niger* ve *Candida* suşları ile mücadelede etkinliğini göstermiştir.

Ayrıca çalışmalar, *Melia azedarach*'ın çeşitli viral patojenlerin gelişimini inhibe ettiğini göstermiştir. Bu aktivite, "meliasin" bileşiği ile ilişkilendirilmiştir ve antiviral ajanların geliştirilmesinde öncü madde olarak düşünülmektedir. *Melia azedarach*'ın antileishmanial aktivitesi üzerine yapılan çalışmalar mevcuttur. *Leishmania* parazitinin neden olduğu Leishmaniasis, dünyanın birçok yerinde yaygın olarak görülen bir parazit hastalığıdır. *Melia azedarach*'tan elde edilen ekstraktlar *Leishmania* parazitlerine karşı önemli aktivite göstermiştir; bu aktivite “azadiraktin” bileşiği ile ilişkilendirilmiştir.

Ayrıca *Melia azedarach*'ın çeşitli parazitlere karşı anti-helmintik etkinlik göstermesi, bu enfeksiyonlarla mücadelede olası bir rolü olabileceğini düşündürmektedir.

Melia azedarach'ın bir diğer dikkate değer biyolojik aktivitesi de "antioksidan" kapasitesidir. Oksidatif stres, kardiyovasküler bozukluklar, nörodejeneratif durumlar, Alzheimer ve kanser dahil olmak üzere çeşitli hastalıklarda çok önemli bir rol oynar. Çeşitli çalışmalarda gösterildiği gibi *Melia azedarach*, serbest radikalleri temizleme ve oksidatif stresi azaltma kapasitesine sahiptir. Antioksidanlar, reaktif oksijen türlerinin neden olduğu hasara karşı hücreleri korumada çok önemli bir rol oynar ve böylece potansiyel olarak oksidatif stres ile ilişkili çeşitli hastalıkların önlenmesine veya yönetimine katkıda bulunur. Çalışmalar, *M. azedarach*'ın antioksidan aktivitesinden içeriğindeki fenolik bileşikler sorumlu tutmaktadır.

Melia azedarach'ın anti-inflamatuar etkileri ile ilgili olarak da birçok çalışma yapılmıştır. Enflamasyon, çeşitli hastalıkların patogeneğinde yer alır ve bitkinin özleri, proinflamatuar enzimlerin inhibisyonu, inflammatuar sitokinlerin düzenlenmesi, antioksidan özellikler ve bağışıklık tepkilerinin modülasyonu yoluyla enflamasyonu azaltma yeteneği göstermiştir. Bu anti-inflamatuar aktivitenin, kronik inflammatuar durumların ve ilgili bozuklukların yönetilmesinde etkileri olabilir. *Melia azedarach*

ekstreleri ağrıyı hafifletme ve ateşi düşürme potansiyeli de göstermiştir. Bu etkiler, çeşitli enfeksiyonlarla ilişkili ağrı ve ateşle ilgili durumların yönetiminde önemlidir.

Ayrıca yapılan araştırmalar, *Melia azedarach* ekstrelerinin kanser hücrelerine karşı sitotoksik etkilerine de odaklanmıştır. Çalışmalar, bitkinin ekstrelerinin çeşitli kanser hücre hatlarına karşı seçici sitotoksikite sergilediğini ve bu da onu yeni antikanser ajanları geliştirmek için potansiyel bir aday haline getirdiğini gösteriyor.

Melia azedarach bitki özleri, ağrıyı hafifletme ve ateşi düşürme potansiyeli göstermiştir. Bu etkiler, çeşitli enfeksiyonlarla ilişkili ağrı ve ateşle ilgili durumların yönetiminde özellikle değerlidir.

Ayrıca araştırmalar *Melia azedarach* ekstrelerinin kanser hücrelerine karşı sitotoksik etkilerine de odaklanmıştır. Bitkiden elde edilen ekstrelerin çeşitli kanser hücre hatlarına karşı seçici sitotoksikite gösterdiği belirlenmiştir. Yeni antikanser ajanların geliştirilmesinde potansiyel aday olabileceği düşünülerek antikanser etkiden sorumlu bileşiklerinin araştırılması gerekmektedir.

M. azedarach ekstrelerinin biyolojik aktiviteleri ve fitokimyasal bileşiminin aydınlatılmış olması fitoterapide kullanımının optimize edilmesi açısından önemlidir. Bu araştırma, *M. azedarach*'ın fitoterapideki önemine dair giderek artan bilgi birikimine katkıda bulunurken, gözlenen etkilerden sorumlu olan belirli biyoaktif bileşenleri ortaya çıkarmak için daha fazla araştırma yapılması gerektiği ortaya çıkmıştır.

Anahtar kelimeler: Tıbbi bitkiler, *Melia azedarach*, biyolojik aktiviteler, fitokimyasal bileşim, *Melia azedarach*'ın fitoterapideki önemi

ABSTRACT

Eswiei, Khawla (2023). A review on the evaluation of the biological activities of the *Melia azedarach* and its importance in phytotherapy. Istanbul University, Faculty of Pharmacy, Department of Pharmacognosy. Master Thesis. Istanbul.

Medicinal plants have been widely recognized and utilized for centuries due to their therapeutic properties and potential in treating various ailments. These plants offer a vast array of bioactive compounds that can exert beneficial effects on human health. One such plant of considerable interest is *Melia azedarach* (Meliaceae family) commonly known as the Chinaberry tree. *Melia azedarach* have a lengthy history of being used traditionally as medicine by numerous civilizations worldwide. Studies have revealed that *Melia azedarach* possesses antimicrobial, anti-inflammatory, antioxidant, anthelmintic, antitumor, analgesic, and antipyretic and cure wounds. These properties are attributable to the existence of various phytochemicals in the plant, such as alkaloids, flavonoids, and phenolic acids. The findings of this study emphasize the therapeutic potential of *Melia azedarach* in phytotherapy. By understanding its biological activities and phytochemical composition, the utilization of *Melia azedarach* can be optimized for the development of natural medicines. This research contributes to the growing body of knowledge on the importance of *Melia azedarach* in phytotherapy and highlights the need for further investigation and exploration of its potential applications, elucidate the underlying mechanisms of action, and identify specific bioactive components responsible for the observed effects.

Key words: Medicinal plants, *Melia azedarach*, biological activities, phytochemical composition, importance of *Melia azedarach* in phytotherapy,

2. INTRODUCTION

2.1. Phytotherapy and importance of medicinal plants in phytotherapy

The term of "phytotherapy" come from the Ancient Greek word "phyto" which mean "plant" and "therapy" which meaning "treatment". Phytotherapy utilizes medicinal plants or plant extracts for therapeutic purposes. It involves the use of therapeutic botanicals to prevent, cure, or alleviate a variety of health conditions. In phytotherapy, various plant components including flowers, stems, leaves, roots, and bark may be used to prepare remedies. These plant materials contain bioactive compounds that have medicinal properties and can affect the body in different ways. The bioactive compounds may include alkaloids, flavonoids, terpenoids, phenolic compounds, and many others (1).

It was a French physician "Henri Leclerc", who coined the term of phytotherapy in 1913 and produced several editions of the *Précis de phytothérapie* ("Handbook of Phytotherapy"), the first of which was published in 1922, is credited with developing the idea of phytotherapy. The phrase "herbal treatment" or "treatment with medicinal herbs" is now used to describe these practices (2).

Medicinal plants play a crucial role in phytotherapy, as they have natural healing properties, which stem from the bioactive compounds present in their various parts. These compounds possess therapeutic effects such as anti-inflammatory, antimicrobial, antioxidant and immunomodulatory properties. These activities make them valuable in the prevention and management of diseases. Compared to many synthetic pharmaceutical drugs, medicinal plants often have fewer adverse side effects. This is because they typically contain a combination of active compounds that work synergistically, minimizing the risk of toxicity. However, it is important to note that herbal remedies can still have interactions and side effects with each other or with medication, therefore caution and proper guidance are necessary (3).

Medicinal plants are characterizes by easily accessible and cost-effective, making them viable healthcare options, particularly in regions with limited access to modern medical facilities. Ongoing scientific research contributes to advancing the field of phytotherapy, unveiling the chemical composition, mechanisms of action, and therapeutic potential of medicinal plants. However, it is vital to use of medicinal plants

correctly in term of dosage, method of use and treatment period. Lastly in summary, the significance of medical herbs in phytotherapy is duo to their natural healing properties, cultural significance, accessibility, diverse treatment options, and contributions to healthcare advancements (2).

2.2. The importance of the *Melia azedarach* in phytotherapy

The use of medicinal plants in phytotherapy is profiting a lot of interest due to its possible therapeutic advantages and negligible side effects. Among these plants, is the *Melia azedarach* plant that holds great importance in the field of phytotherapy. This plant has been utilized for centuries in traditional medicine systems in various cultures for treating a diverse range of ailments, including skin disorders, gastrointestinal issues, fever and inflammation this is due to its various medicinal properties (4).

The various parts of *Melia azedarach*, including the seeds, leaves, roots and fruits, have a variety of bioactive substances including alkaloids, flavones, terpenoids, anthraquinones and terpenoids. These phytochemical constituents contribute to the plant's remarkable therapeutic potential (4).

The primary reasons for the importance of *Melia azedarach* in phytotherapy is its antimicrobial activity against various types of bacteria, fungi, and parasites. In addition to its antimicrobial properties, *Melia azedarach* has been found to possess antioxidant activity, anti-inflammatory activities and antitumor activities.

Furthermore, *Melia azedarach* extracts have shown insecticidal activity and therefore, it can be used as an alternative to synthetic chemical pesticides, possessing insecticidal and ant parasitic properties that can help control pests and parasites in a more environmentally friendly manner (5).

2.3. Historical background

The term "medicinal plants" refers to plants or sections of plants that contain active substances (secondary metabolites) such as glycosides, alkaloids, flavonoids, tannins, phenolic compounds and etc. They are administered orally, inhaled or directly applied in the skin for medical purpose (6).

Throughout time, human beings used natural resources for their fundamental necessities, including nourishment, clothes, fertilizer, medicines, scents, and other household goods and methods of transportation (7).

Medical herbs have been used since ancient times, with evidence of their use in various cultures throughout history. By trial and error, ancient man began to differentiate which plants are helpful and which are plants that are toxic. Over time, different cultures have developed their own systems of herbal medicine, which have been passed down through generations (8).

Herbal medicine has been used for thousands of years by various cultures throughout the world, including the Sumerians, Egyptians, Greeks, Chinese's, Romans, Indians, and etc. Many of these cultures relied on herbal medicine as their primary form of healthcare, and herbal remedies were often the only treatment available for a range of conditions (9).

2.3.1. Sumerian

The earliest known record of medicinal plant use comes from the Sumerians in Mesopotamia, dating back to around 2600 BC. who created clay tablets detailing the use of over 250 different plants for medicinal purposes. Some of the plants that have been utilized include "*Cupressus sempervirens*", "*Papaver somniferum*" and "*Commiphora myrrha*" (8).

2.3.2. Ancient Egyptians

The ancient Egyptians were among the first civilizations to document their use of medicinal plants. They recorded their knowledge on papyrus scrolls, such as the "Ebers Papyrus", the "Edwin Smith Papyrus" and the "Kahun Gynaecological Papyrus", which are considered some of the earliest known medical texts which dating back to around 1550 BC. The ancient Egyptians relied on medicinal plants for wide range of ailments including digestive issues, respiratory problems, and skin conditions. Some of the commonly used plants include aloe vera, garlic, coriander, and frankincense (9).

2.3.3. Ancient Greece

In ancient Greece, medicinal plants were used extensively by physicians such as Hippocrates and Galen. Hippocrates, known as the "father of medicine," used medicinal plants around 400 BC. in his practice. Greek herbal treatments were frequently used in conjunction with diet, physical activity, and other therapeutic techniques to treat ailments and sustain general health (10).

2.3.4. Traditional Chinese Medicine (TCM)

For centuries, "Traditional Chinese Medicine" (TCM) has served as an encompassing medical system deeply rooted in Chinese culture for over 2,000 years. It is based on the principles of yin and yang, and the concept of qi (vital energy) flowing through meridians in the body. In traditional Chinese medicine, the use of medicinal plants dates back to 200 BC. The earliest known Chinese pharmacopoeia, the Shennong Bencao Jing, lists over 365 medicinal plants and their uses. The herbal remedies used in TCM had recorded in classical texts, such as "Compendium of Materia Medica" and "Shennong's Classic of Materia Medica" (8-9).

2.3.5. Ayurvedic Medicine (Indian Traditional Medicine):

The Indian term Ayurveda, which translates to "Science of Life," comes from the terms Ayar (life) and Veda (knowledge or science). Ayurveda, a holistic system of medicine, has been practiced for centuries and is depend on using natural therapies, such as medicinal herbs, to promote health and treat various ailments. The utilization of medicinal herbs in Ayurvedia has been documented in historic writings, including the "Charkas Samhita" and "Sushruta Samhita", which are considered foundational texts of Ayurveda. The Charaka Samhita, an ancient Ayurvedic text dating back to the 6th century BC, describes the use of numerous medicinal plants for treating various ailments, including digestive disorders, respiratory conditions, skin diseases, and more. For example, it mentions the use of ginger (*Zingiber officinale*) for digestive issues, turmeric (*Curcuma longa*) for inflammation, and neem (*Azadirachta indica*) for skin ailments. The Sushruta Samhita, another ancient Ayurvedic text, focuses on surgical procedures and also mentions the application of herbal remedies to treat illness. It

describes the use of plants such as aloe vera (*Aloe barbadensis*) for wound healing, garlic (*Allium sativum*) for cardiovascular health, and ashwagandha (*Withania somnifera*) for its rejuvenating properties. Additionally, the Rigveda, an ancient Indian scripture dating back to around 1500 BC, mentions the use of several medicinal plants, including holy basil (*Ocimum sanctum*) for respiratory issues and brahmi (*Bacopa monnieri*) for enhancing memory and cognitive function (9).

2.3.6. Traditional American Medicine

American usage of medicinal plants in America can be traced back to the indigenous peoples who have been using plants for medicinal purposes for thousands of years. Native American tribes used plants such as Echinacea, goldenseal, ginseng, wild yam, black cohosh, and passionflower for a variety of ailments. They also developed their own traditional medicine systems, which were based on a holistic approach to healing that emphasized the connection between the physical, emotional, and spiritual aspects of a person. In the 19th century, the use of medicinal plants in America began to decline as synthetic drugs became more widely available. However, there were still some practitioners who continued to use herbal remedies, and the popularity of herbal medicine began to increase again in the late 20th century (9).

2.3.7. European Traditional Medicine

Europe has a rich history of medicinal plant usage that dates back to ancient times. Many early European civilizations, such as the Greeks and Romans, documented the use of medicinal plants in their writings. European monasteries during the middle Ages also played a significant role in preserving and cultivating medicinal plants, as monks used them to treat the sick. Examples of notable medicinal plants from Europe include St. John's Wort for mood disorders, chamomile for digestive issues, and valerian for anxiety and sleep disorders (9).

2.3.8. Ancient African Medicine

Africa has employed herbal treatments for thousands of years and continues to play a vital role in traditional African medicine. Indigenous tribes and cultures across Africa have a deep understanding of the medicinal properties of various plants and use them for the treatment of a variety of conditions, including malaria, digestive issues, and skin ailments. Many African medicinal plants have also been incorporated into modern pharmaceuticals. For example, African cherry tree bark "*Prunus Africana*" is utilized to produce quinine, a drug used to treat malaria. Other notable African medicinal plants include rooibos "*Aspalathus linearis*" for its antioxidant properties, devil's claw "*Harpagophytum procumbens*" for its anti-inflammatory effects, Artemisia afra "*African wormwood*" for common cold and chest problems and African ginger "*Siphonochilus aethiopicus*" for its digestive benefits (9).

2.4. Natural products are potential sources of new drug leads

The use of medicinal plants has continued to the present day, with many plant-based remedies still in use in traditional medicine systems around the world. According to a report by the "World Health Organization" (WHO), around 80% of individuals in underdeveloped nations rely on conventional therapies for their basic medical requirements. Whereas due to their affordability, accessibility, and safety, medications produced from plants are frequently used (11).

The dependence of people on the plants for survival provides the researchers guides to discovery and development of new pharmaceuticals (12).

There is a wide range of products derived from medicinal plants available in the market. These products found in various forms, including herbal supplements, herbal teas, essential oils, natural skincare and cosmetic products (13).

2.5. Aim and objective of the study

This study's objective is to conduct a comprehensive review of the existing literature on the biological activities and chemical composition of *Melia azedarach*, as well as its current usage in phytotherapy, in order to determine the need for further research or not.



3. MATERIALS AND METHODS

3.1. Review of Literature

A thorough search of existing literature was performed to identify relevant articles pertaining to the biological activity of *Melia azedarach* and its importance in phytotherapy. Electronic databases, including PubMed, Science Direct and Google Scholar, have been researched using keywords such as "*Melia azedarach*," "biological activity," and "phytotherapy." The search was limited to articles published in English

3.2. Selection Criteria

The selection of articles was based on predefined inclusion and exclusion criteria. Inclusion criteria encompassed studies investigating the biological activity of *Melia azedarach*, including its pharmacological properties, mechanisms of action, and therapeutic applications in phytotherapy. Exclusion criteria included studies on other plant species or unrelated topics.

4. FINDINGS

4.1. Botanical Description

4.1.1. Taxonomic classification of *Melia azedarach*

Kingdom: Plantae

Subdivision: Angiospermae

Order: Sapindales

Family: Meliaceae

Genus: *Melia*

Species: *azedarach*

4.1.2. Meliaceae family

Usually it would be trees or shrubs, rarely subshrubs, are a diverse group of flowering plants that includes approximately 50 genus and over 550 species, distributed throughout the world (14).

4.1.3. *Melia* genus

Deciduous trees or shrubs with hard wood. A genus of about 15 species chiefly in south Asia and Australia represented here by 1 cultivated species (14).

4.1.4. Geographical distribution

Melia azedarach has a broad geographical distribution, spanning multiple countries and continents including, Asia, India, China, and Southeast Asian countries, Africa, Australia, Europe, and the Americas. Thanks to its adaptability to different climates (14).



Figure 1: World map distribution of *M. azedarach*

(<https://www.discoverlife.org/mp/20m?map=Melia+azedarach>)

4.1.5. Botanical description of *Melia azedarach*

Perennial deciduous tree, grown throughout warm countries, medium-sized tree that typically grows to a height of 10-15 meters, but can occasionally reach up to 20 meters. It has a spreading, rounded crown and an open branching pattern. The age and growing circumstances of the tree can affect the trunk diameter. Although it can occasionally attain higher diameters in extreme situations, mature specimens normally have trunk diameters ranging from 30 to 60 centimeters (4).



Figure 2: *Melia azedarach* L. (general view)

(<https://alchetron.com/Melia-azedarach>)

4.1.5.1. Leaf

The leaves are alternate, compound, and pinnately divided. Each leaf is composed of 9 to 17 leaflets arranged in an alternate fashion. The leaflets are ovate to lanceolate in shape, with serrated edges and a glossy green color. The leaves turn yellow or yellowish-brown before falling in autumn (4).



Figure 3: *Melia azedarach* L. (leaves)

(<https://www.istockphoto.com/tr/foto%C4%9Fraf/margosa-nim-or-neem-tree-genus-melia-green-leaf-isolated-gm626458560-110637659>)

4.1.5.2. Flowers

Flowers actinomorphic, bisexual rarely unisexual, Calyx 4-5, petals 4-5, stamen 8-10 or rarely many. Flowers are purple and fragrant (4).



Figure 4: *Melia azedarach* L. (flowers)

(<http://www.rnr.lsu.edu/plantid/species/chinaberry/chinaberry.htm>)

4.1.5.3. Fruit

The tree produces spherical fruits known as drupes. These fruits are about 1 cm in diameter and initially green, turning yellow or yellowish-orange when ripe. Each fruit contains a hard, single seed. The fruits persist on the tree throughout winter (4).



Figure5: *Melia azedarach* L. (fruits)

(https://keys.lucidcentral.org/keys/v3/eafrinet/weeds/key/weeds/Media/Html/Melia_azedarach_%28Melia%29.htm)

4.2. Traditional uses of *Melia azedarach*

Melia azedarach has a rich history of traditional uses across different cultures. Table 1 provides a comprehensive overview of the various traditional applications associated with *M. azedarach*, plant part used and method of application. (4-5, 15-16).

Table 1. Traditional uses of *Melia azedarach*

Plant part	Traditional uses	Method of application
Leaves	Diuretic, anthelmintic, effective in skin diseases like leprosy, chicken pox, smallpox, hysteria. Toothache, headache, fever, rheumatic pain, malaria, gingivitis, piles, pyrexia and insecticide.	Externally for burns. Internally and externally in skin diseases. Used externally like compresses to alleviate both headaches and fever. Mouth wash in gingivitis and toothache. Internally in anthelmintic, diuretic, and expectorant.

Stems	Spleen enlargement, asthma, general debility, antispasmodic, antiviral, gonorrhoea, tiredness, cough and loss of appetite.	Internally
Fruits	For the treatment of diabetes, purgative, emollient, antihemorrhoidal, and anthelmintic.	Internally
Flowers	Bacterial skin diseases, astringent, diuretic, anthelmintic, cough, anodyne, stomachic and killing lice	Internally and externally
Seeds	Malaria fever, leprosy, scrofula, helminthiasis, rheumatism and in pelvic region pain	Internally and externally
Roots	Astringent, anodyne, antiseptic, anthelmintic, constipating, expectorant, febrifuge, cough, asthma lumbago, leprosy, dysmenorrhoea, diabetes and abnormal urethral discharge.	Internally and externally
Barks	Antidiarrhoeal, diuretic, rheumatic pain, fever, overall debilitation, stomach upset and gonorrhoea.	Internally

4.3. Chemical composition of *Melia azedarach*

The chemical composition of *M. azedarach* is complex. The biological activities of *Melia azedarach* attributed to chemical compounds with medicinal properties. These compounds were classified according to their chemical structures and presence in the plant parts as showed in Table 3 (4- 5, 15-19).

Table 2. Chemical compounds of *Melia azedarach*

Name of the compound	Plant parts used
Phenolic compounds (Flavonoids, Lignin's, flavones and phenolic glycosides)	
1-Cinnamoyl-3-methacrylyl-11-hydroxy meliacarpin	Leaves
1,3-dicinnamoyl-11-hydroxy-rneliacarpin	Leaves
Kaempferol	Leaves
Kaempferol-3-O- β -rutinoside	Leaves
Quercitrin	Leaves
Quercetin-3-O- β -rutinoside	Leaves
Rutin	Leaves
Deacetylsalannin	Leaves
4,5-Dihydroxy flavone-7-O-u-Lrhamnopyranosyl-(1-4)- β -D-glucopyranoside	Leaves
Vanillin	Stems
Apigenin-5-O- β -D-galactopyranoside	Fruits and seeds
Pinoresinol	Roots
Chlorogenic acid	Fruits
Terpenes	
α -Pinene	Leaves and stem
α -Terpinene	Leaves and stem

β -Pinene	Leaves and stem
Nimbinene	Leaves and seeds
α -Terpineol	Leaves
7 Acetoxy-14 β ,15 β -epoxygedunanol-ene-3-O- β -D-glucopyranoside	Stems
3 Hydroxyeupha-7,24-diene-21,16-olide	Stems
1,12-Diacetyl trichilin-B	Roots
Pyroangolensolide	Barks
Coumarins	
Scopoletin	Stems
1-Tigloyl-3,20-diacetyl-11-methoxymeliacarpinin.	Roots
1-Deoxy-3- methacrylyl-11-methoxy meliacarpinin	Roots
1-Cinnamoyl-3-hydroxy-11-methoxy meliacarpinin	Roots
Glycosides	
3-O- α -L-rhamnopyranosid	Stems
1,5-dihydroxy-8-methoxy-2-methyl anthraquinone-3-O- α -L-rhamnopyranoside	Stems
β -Sitosterol B-D-glucoside	Roots
7- α -acetoxy-14 β -15 β -epoxygedunanol-1-en-3-O- β -D-glucopyranosid	Stems
6,11 diacetoxy-7-oxo-14 β -epoxymeliacin (1,5-diene-3-O- β -D-glucopyranoside)	Seeds
Anthraquinones	

1,8-dihydroxy-2-methyl anthraquinone-3-O- β -D, Methylkuronate,	Stems
1,3,5,8-Tetrahydroxy-2-methyl anthraquinone	Stems
1,5-dihydroxy-8-methoxy-2-methylanthraside	Stems
Alkaloids	
4-methoxy-1-vinyl-beta-carboline	Stems
4,8-dimethoxy-1-vinyl-beta-carboline	Stems
Limonoids	
Nimbolinin B and 1-desacetylnimboline B	Fruits
Nimboldins A and B,	Fruits and roots
triterpene B,	Fruits
meliacins A1, A2, B1, B2,	Fruits
sendanin	Fruits
Sendenal	Fruits
1-cinnamoylmelianolone	Fruits
Melianone	Fruits
1-O-Deacetyl ohchinolide-B	Fruits
1-Deacetylnimbolinin A	Fruits
3-Deoxymelian one	Fruits
29-Deacetyl sendanin	Fruits
Meliatoxin-B2	Fruits
11-dihydroxymeliacal-1	Fruits

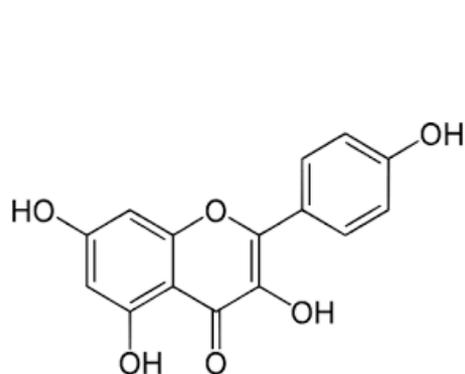
Azadirachtin-A	Fruits
Azedarachin-A	Roots
12-O-Acetyl azedarachin-A and B	Roots
Cinnamoylemelianolone	Fruits
Gedunin	Fruits
15-O-deacetylnimboldine	Fruits
3-Epimelianol	Fruits
Azedarachin-C	Roots
12-O-Acetyl trichilin-B	Roots
7,12-Diacetyl trichilin-B	Roots
29-Isobutylsendanin	Roots
1-Deacetyl nimbolinin-B	Roots
2-O-Acetyl azedarachin-B	Roots
2 α -Acetyl-29-deacetyl-29-isobutyryl sendanin	Roots
Meliacarpin	Seeds
1,12-Diacetyl trichilin-B	Seeds
12 α - acetoxy fraxinellone	Roots
Azedaralide	Barks
9 alpha-acetoxyfraxinellone	Barks
15-O-deacetylnimboldine	Barks
Salannin	Fruits and roots
Triterpenes	

α -spinasterone	Fruits
Sugiol	Fruits
21,23,24,25-Diepoxy-tirucall-7-ene-21-ol	Fruits
3-Epimelianol	Fruits
Terpenoids (Diterpenoids Triterpenoid, Tetranortriterpenoids, sesquiterpenoids)	
3-Deoxy melianone	Fruits
1,12-Diacetyl trichilin-B	Roots
Salannal	Roots
Trichilin-B and Trichilin H	Roots
24-Methylenecydoartanone	Roots
24-Methylenecycloartanol	Roots
Trichilin-D	Roots
Sugiol	Seeds and fruits
3- β ,7 α -Dihydroxy-21,23-epoxy apotirucalla-14,24-diene-21-one	Seeds
Melianolmeliacin	Seeds
Tingenone	Seeds
Kulinone	Seeds and barks
Fatty acids	
Stearic acid	Fruits
Octadecanoic acid	Fruits
Palmitic acid	Leaves

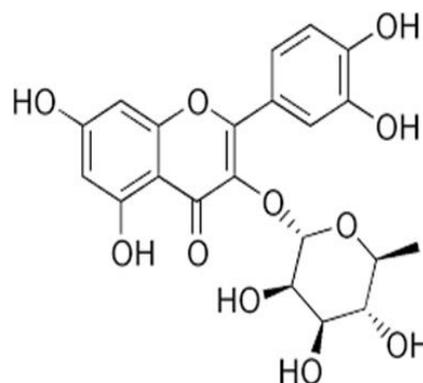
Linoleic acid	Roots and seeds
Linolenic acid	Roots and seeds
9-octadecenoic acid	Roots
Oleic acid	Seeds
Methyl 3,12-dihydroxyhexadecanoate	Seeds
Sterols	
6- β -Hydroxy-4-Stigmasten-3-one	Roots
β -Sitosterol- β -D-glucoside	Roots
Campesterol	Roots and seeds
4-Stigmastanen-3-one	Roots
4-Campestene-3-one β -Sitosterol	Roots
Daucosterol	Seeds
Stigmasterol	Seeds
β -sitosterol	Seeds
Carboxylic acids	
Vanillic acid	Roots and seeds
Cinnamic acid	Roots
Trans-cinnamic acid	Roots
Benzoic acid	Seeds
1-methyl-1H-pyrrole-2-carboxylic acid	Fruits
Amino acids	
Cystine	Seeds

Serine	Seeds
Arginine	Seeds
Glycine	Seeds
Glutamic acid	Seeds
Threonine	Seeds
Methionine	Seeds
Leucine	Seeds
Lycine	Seeds
Proline	Seeds

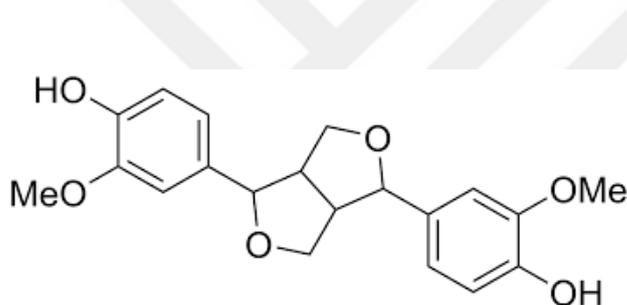
3.3.1. Chemical structures of some phenolic compounds



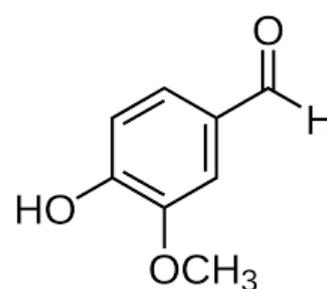
Kaempferol



Quercitrin

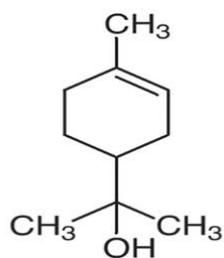
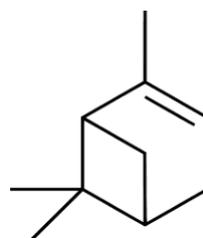
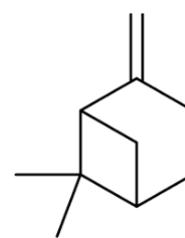


Pinoresinol

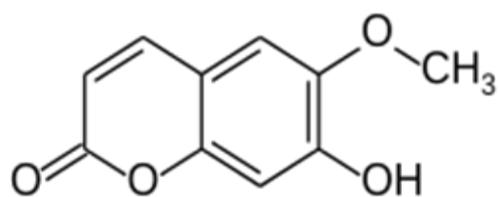


Vanillin

4.3.1. Chemical structures of some terpenes

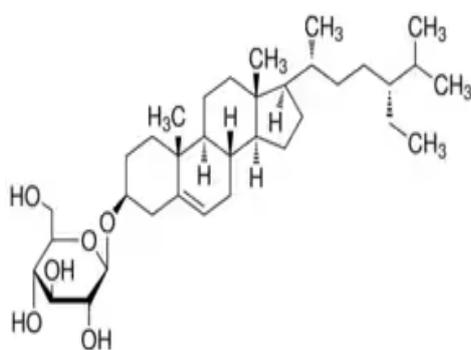
 α -Terpineol α -Pinene β -Pinene

4.3.2. Chemical structures of some coumarins



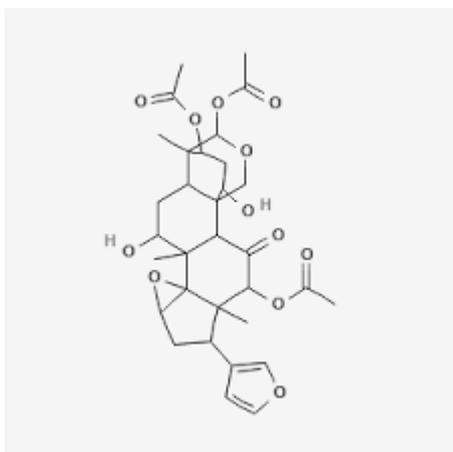
Scopoletin

4.3.3. Chemical structures of some glycosides

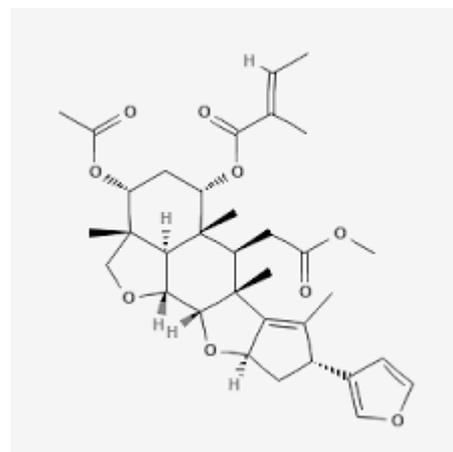


β -Sitosterol β -D-glucoside

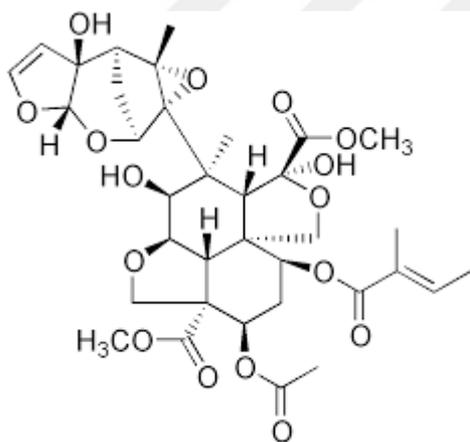
4.3.4. Chemical structures of some limonoids



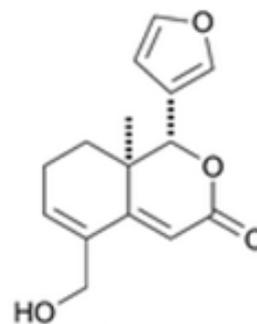
Sendanin



Salannin

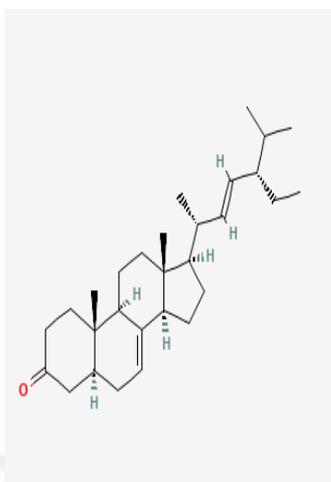


Azadirachtin



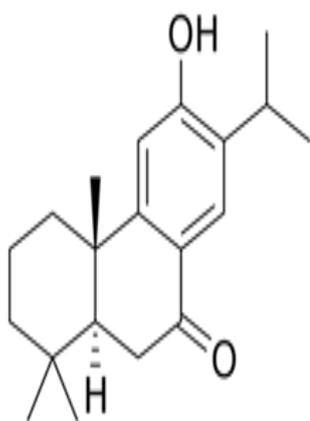
Azedaralide

4.3.5. Chemical structures of some triterpenes

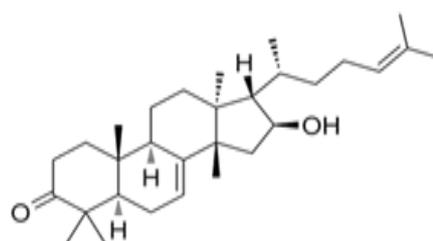


α -spinasterone

4.3.6. Chemical structures of some terpenoids

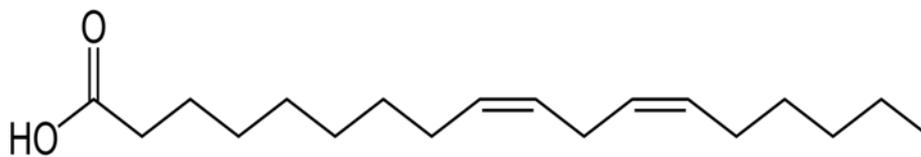


Sugiol

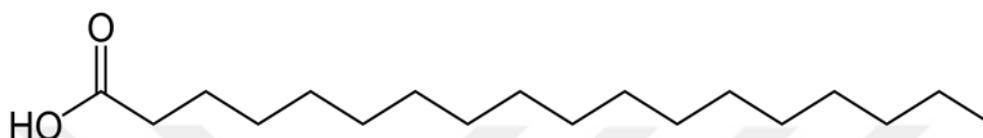


Kulinone

4.3.7. Chemical structures of some fatty acids

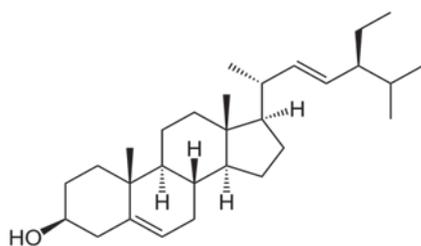


Linoleic acid

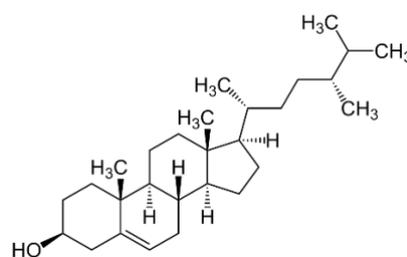


Stearic acid

4.3.8. Chemical structures of some sterols

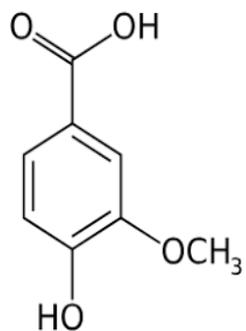


Stigmasterol

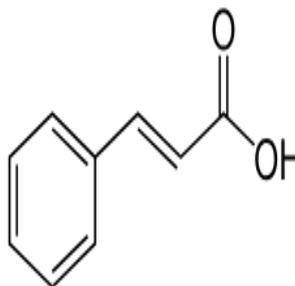


Campesterol

4.3.9. Chemical structures of some carboxylic acids

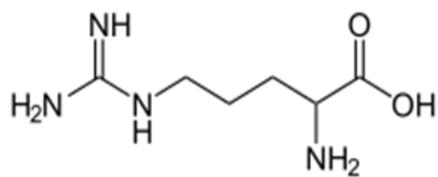


Vanillic acid

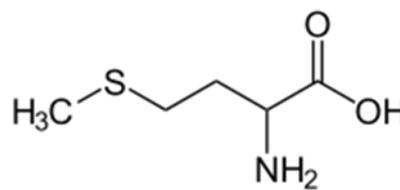


trans-Cinnamic acid

4.3.10. Phytochemical structures of some amino acids



Arginine



Methionine

4.4. Pharmacological activities of *Melia azedarach*

4.4.1. Antibacterial and antifungal activities

A study was published in 2016 by Nazar et al. on the antibacterial activity of *Melia azedarach* fruits that had been collected from Iraq against "*Bacillus subtilis*", "*Proteus*", "*Pseudomonas aeruginosa*", "*E. coli*", "*Staphylococcus aureus*" and "*Klebsiella*." The results showed that both aqueous and alcohol extracts of *Melia azedarach* fruit exhibited significant antibacterial activity against the tested bacteria (20).

A study was published in 2012 by Mohamad amin et al. on the antibacterial activity of seeds, fruits, leaves, and flowers of *Melia azedarach* that had been collected from Iran against "*Xanthomonas campestris pv. Campestris*", "*Pseudomonas syringae pv. Syringae*" and "*Rathayibacter tritici*." That destroy agriculture crops.

The results showed that parts of the plant that were extracted by methanol have an antibacterial effect against both gram-positive and gram-negative plant pathogens. Notably, the seed-fruit extracts exhibited higher levels of antibacterial activity compared to the extracts from other plant organs (21).

A study was published in 2019 by Kathiresan et al. on the antibacterial activity of *Melia azedarach* leaves that had been collected from India and extracted by ethanol, methanol, and acetone against various pathogenic bacteria and fungi.

The results showed that the ethanol extract is more effective compared to other extract. The zone of inhibition of the ethanol extract was 12 mm against both "*Escherichia coli*" and "*Pseudomonas aeruginosa*", 14 mm against both "*Vibrio cholera*" and "*Klebsiella pneumoniae*", 15 mm against "*Staphylococcus aureus*", and 16 mm against "*Bacillus subtilis*". Furthermore, the ethanol extract show its effectiveness against both "*Aspergillus niger*" and "*Candida albicans*" (22).

A study was published in 2016 by Abdul Viqar et al. on the antibacterial activity of *Melia azedarach* seeds that had been collected from India and extracted by aqueous, methanol, ethyl acetate, benzene and petrol solvents at different concentrations (1, 2, 5,

10, and 15 mg/mL) against 18 types of gram-positive and gram negative bacteria isolated from hospital that cause human pathogenic.

The results showed that the extract from ethyl acetate showed the greatest amount of inhibition compared all the extracts against all tested pathogens, particularly affecting on "*Staphylococcus aureus*", "*Bacillus subtilis*" (gram-positive), and "*Pseudomonas aeruginosa*" and "*Shigella flexneri*" (gram-negative). Additionally, methanol extract was efficient against all bacteria, with "*Plesiomonas shigelloides*" and "*Shigella dysenteriae*" showing the highest levels of inhibition. All of the pathogenic bacteria that were examined showed a moderate level of sensitivity to the aqueous extract. The petrol extract exhibited effectiveness against six gram-positive and nine gram-negative pathogenic bacteria, with the highest inhibition observed against "*Bacillus subtilis*", "*Proteus mirabilis*", and "*Shigella flexneri*". Benzene extract inhibited the growth of three gram-positive and nine gram-negative pathogens, with the maximum inhibition zone recorded against "*Shigella flexneri*" and "*Proteus mirabilis*" (23).

4.4.2. Antiviral activity

A study was published in 2009 by Erina et al. on the antiviral activity of "meliacine" compound, derived from *Melia azedarach* leaves in a mouse model of genital herpes infection were examined. Female mice were given intravaginal injections of meliacine after being exposed to MS strains of the Herpes Simplex Virus type 2.

The results showed that the severity of sickness was attenuated in the treated mice, accompanied by reduced virus shedding in vaginal fluids. Moreover, "Meliacine" administration resulted in increased levels of Interferon-gamma (IFN- γ) and Tumor necrosis factor alpha (TNF- α) in the vaginal secretions compared to the infected mice that did not receive treatment. Additionally, the quantity of virus that migrated to the brain was reduced in the "Meliacine"-treated group. These findings suggest that meliacine may hold promise as a potential alternative therapeutic agent for managing HSV-2 genital infection (24).

A study was published in 2023 by Bahaa et al. on the antiviral activity of *Azadirachta indica* and *Melia azedarach* leaves extracted with methanol on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a strain of coronavirus that causes COVID-19 (coronavirus disease 2019) in vitro.

The results showed that both extracts inhibit replication of SARS-CoV-2 virus in vitro at IC₅₀ concentrations 8.451 µg/mL for *Azadirachta indica* and 6.922 µg/mL for *Melia azedarach*. In this study, it is believed that the antiviral activity of *A. indica* and *M. azedarach* plants is due to presence of phenolics and flavonoids (25).

4.4.3. Antileishmanial activity

A study was published in 2014 by Imran Khan et al. on the antileishmanial effect of *Melia azedarach* was evaluated using green fruit extract and ripe fruit extract collected from Pakistan. The study focused on "*Leishmania tropica*" and employed an in vitro promastigote assay, with Amphotericin B used as the reference drug.

The results showed that the green fruits had high activity against Leishmaniasis compared to ripe fruits. where the LC₅₀ value for the green fruits was 0.49 µg/mL, while the LC₅₀ value for the ripe fruits was 8227.5 µg/mL. In comparison, the LC₅₀ value of Amphotericin B was determined as 0.39 µg/mL. The enhanced activity observed in the green fruits may be because to high levels of lemonoids and azadirachtin (26).

A study was published in 2011 by Kawther et al. on the antileishmanial effect of *Melia azedarach* was evaluated using ripe fruit aqueous extract collected from Arbil. The study focused on "*Leishmania donovani*" and employed an in vitro Promastigote assay to assess the leishmanicidal activity of *Melia azedarach* fruits on various biochemical parameters in the liver of mice infected.

The results showed that the ripen fruits of *Melia azedarach* resulted in an elevation of alanine transaminase (ALT) and aspartate transaminase (AST) levels, however, lactate

dehydrogenase (LDH) and alkaline phosphatase (ALP) levels decreased. These results demonstrate that the extract of *Melia azedarach* has potential leishmanicidal capabilities, effectively suppressing the growth of parasites in laboratory mice (27).

4.4.4. Antimalarial activity

According to a study by Charturvedi et al. in 2006, the antimalarial activity of methanol extracts obtained from the leaves, bark, and fruits of *Melia azedarach* was assessed using experimental mice infected with the malaria parasite "*Plasmodium berghei*." The study utilized Chloroquine as a reference drug for comparative analysis.

The results of the study demonstrated that the extracts derived from the fruits and bark exhibited substantial reduction in parasitemia during the early stages of infection. Although the leaf extract also displayed a suppressive effect, it did not reach statistical significance. In the chronic phase of the infection, both the fruit and bark extracts exhibited notable suppressive effects after 5 days of administration. By day 9, these extracts showed significant reduction in parasitemia, albeit to a lesser extent compared to Chloroquine (28).

According to a study by Selvaraj et al. in 2011, the antimalarial activity of leaf extract and fruit extract of *Melia azedarach* was assessed against different species of malarial vectors, including "*Aedes aegypti*," "*Anopheles stephensi*," and "*Culex quinquefasciatus*," under laboratory conditions. The leaves of *Melia azedarach* were collected from India.

The results demonstrated that both the fruit and leaf extracts of *Melia azedarach* exhibited potent larvicidal activity against the mosquito species known to be malarial vectors (29).

4.4.5. Anti-Alzheimer activity

Alzheimer's disease (AD) is a neurodegenerative disorder that progresses over time, leading to impaired brain function and memory deficits. The condition is associated with the accumulation of β -amyloid aggregates and impaired neurotransmission of Acetylcholinesterase. As a result, therapeutic agents with anti-amyloidogenic and

anticholinesterase properties have been recognized as potentially beneficial for treating AD (30).

According to a study by Orhan et al. in 2022 to assess the inhibitory activities of acetylcholinesterase (AChE), butyrylcholinesterase (BChE) associated with Alzheimer's disease, employed an in vitro ELISA assay. The extraction of *Melia azedarach* fruits and leaves was performed using three solvents of varying polarity: ethyl acetate, methanol, and water.

The results demonstrated that the ethyl acetate extract of *Melia azedarach* leaves at concentration 200 µg/mL has high activity to inhibit both AChE and BChE compared to other extracts (31).

4.4.6. Anti-inflammatory activity

In a study conducted by Akacha et al. (2016), the anti-inflammatory activities of the ethanolic leaf extract of *Melia azedarach* were investigated using the carrageenan-induced hind paw edema model in rats, with indomethacin used as the standard drug for comparison.

The results of the study demonstrated that the ethanolic leaf extract of *Melia azedarach* exhibited significant inhibition of carrageenan-induced paw edema, comparable to the effects of indomethacin. The extract, administered at a dose of 150 mg/kg, displayed the highest anti-inflammatory activity, reducing paw edema by approximately 25% after 2 hours of treatment. In comparison, indomethacin at a dose of 10 mg/kg showed a reduction of around 32% (32).

In a study published by Gagan et al. in 2015, the anti-inflammatory activity of *Melia azedarach* seeds, collected from India, was investigated. Hexane was employed as the extracting solvent. The anti-inflammatory activity was evaluated using carrageenan-induced paw edema and formalin-induced inflammation tests conducted on Wistar rats. Indomethacin was used as a reference drug for comparison.

The results of the study demonstrated that the hexane extract of *Melia azedarach* seeds exhibited significant reduction in carrageenan-induced paw edema 52.77% at a dose of

100mg/kg and 91.66% at dose 200 mg/kg after 72 hours. In comparison, the standard drug “Indomethacin” demonstrated 97.22% inhibition. Additionally, in the formalin-induced paw edema model, the seed extract displayed a reduction in inflammation by 15.21% at doses 100 mg/kg and 20.86% at dose 200 mg/kg (33).

In a study published in 2010 by Vishnukanta et al. , the anti-inflammatory activity of *Melia azedarach* roots, collected from India, was investigated. ethanol was employed as the extracting solvent. The anti-inflammatory activity was evaluated using the carrageenan-induced paw edema test conducted on Swiss albino mice.

The ethanolic extract of *Melia azedarach* roots was orally administered to the mice at doses of 100, 200, and 400 mg/kg body weight. The findings revealed that the ethanol extract of *Melia azedarach* roots exhibited a significant reduction in carrageenan-induced paw edema at all tested doses. Notably, the extract demonstrated reductions of 15.08%, 22.06%, and 26.45% at doses of 100, 200, and 400 mg/kg, respectively. The dose of 400 mg/kg caused the greatest decrease in paw edema (34).

In a study published in 2012 by Singh P et al., the anti-inflammatory activity *M. azedarach* bark was investigated. Ethanol was employed as the extracting solvent. The anti-inflammatory activity was assessed using the carrageenan-induced paw edema model in rats. The ethanol bark extract was orally administered to the rats at doses of 200 and 400 mg/kg body weight, and the paw volume was measured at various time intervals.

The results of the study demonstrated that the ethanol bark extract significantly reduced paw edema induced by carrageenan in a dose-dependent manner. The highest level of inhibition, amounting to 41.84%, was observed at the dose of 400 mg/kg after 3 hours of carrageenan injection (35).

4.4.7. Antioxidant activity

According to a study in 2006 by Mohammed Fazil et al. , the antioxidant activity of *Melia azedarach* leaves collected from India and was extracted with distilled water,

ethanol and petroleum ether. the antioxidant activity was evaluated by using the 2,2-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay.

The findings of the study demonstrated that the ethanol extract of *Melia azedarach* has the most potent radical scavenging activity, with a percentage of $71.42 \pm 0.04\%$. After that came the aqueous extract, which had a scavenging activity of $68.87 \pm 0.09\%$, and the petroleum ether extract with a scavenging activity of $64.76 \pm 0.06\%$. This antioxidant activity of *Melia azedarach* is ascribed to flavonoids and phenolic compounds (36).

In a study published by Adil Munir et al. in 2012, the antioxidant effect of bark, stem, leaves and fruit, of *Melia azedarach* collected from Pakistan was evaluated. The extraction of these plant parts was conducted using methanol as the solvent. The antioxidant activity of sun-dried and air-dried extracts from different parts of *Melia azedarach* was assessed using various in vitro antioxidant assays, including DPPH free radical scavenging activity, Total Flavonoid Contents (TFC), Total Phenolic Contents (TPC), and the percentage inhibition of linoleic acid oxidation.

All experiments showed that the stem bark of *Melia azedarach* had the highest antioxidant activity, with sun-dried samples showing more antioxidant activity than air-dried extracts. The DPPH scavenging activity ranged from 55.43% to 63.86% for sun-dried samples and from 48.54% to 61.00% for air-dried samples. Among these, the sun-dried stem bark exhibited the highest percentage value of 63.87%, while the air-dried fruit displayed the lowest value of 48.54% (37).

In a study published by Imran Khan et al. in 2014, the antioxidant activity of *Melia azedarach* extracts obtained from green and ripe fruits collected from Pakistan was evaluated. The extraction of *Melia azedarach* fruits was performed using distilled water through a maceration method for duration of 6 days. The antioxidant activity of the fruit extracts was assessed using the 2,2-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay.

The results revealed that the green fruit extract exhibited a maximum antioxidant activity of $42.59 \pm 3.12\%$ at the highest concentration of $100 \mu\text{g/mL}$, whereas the ripe fruit extract showed a lower antioxidant activity of $14.66 \pm 1.42\%$ at the same concentration. In comparison, ascorbic acid demonstrated significant activity with an inhibition percentage of $83.23 \pm 1.68\%$ at this concentration. These results indicated

that the antioxidant activity of the plant extract was dose-dependent. Furthermore, the study found that the green fruits contained a higher amount of phenolic compounds, resulting in greater antioxidant activity. This suggests that the green fruit extract possesses a higher proton donating capability and may serve as an effective scavenger of free radicals (25).

In a study published by Gayatri Nahak et al. in 2010, the antioxidant activity of leaves from *Azadirachta indica* and *Melia azedarach*, collected from India, was evaluated. The leaves of both species were extracted using methanol, ethanol and distilled water. The antioxidant activity of the extracts was assessed using the (DPPH) radical scavenging assay.

The results revealed that the ethanol extract had highest antioxidant activity with $68.23 \pm 0.03\%$, proceeded by the aqueous extract with $64.34 \pm 0.04\%$ and methanol extract with $61.17 \pm 0.05\%$. In comparison, the extracts from *Azadirachta indica* displayed lower scavenging activity, with the ethanol extract showing $50.48 \pm 0.03\%$, the aqueous extract showing $49.48 \pm 0.03\%$, and the methanolic extract showing $41.17 \pm 0.04\%$ scavenging activity (38).

In a study published by Khatoon et al. in 2014, the antioxidant activity of *Melia azedarach* bark, collected from India, was evaluated. The barks were extracted using n-hexane and methanol. The antioxidant activity of the extracts was assessed using the 2,2-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay.

The results demonstrated that the n-hexane extract of *Melia azedarach* exhibited higher antioxidant activity compared to the methanolic extract. The IC_{50} values for the n-hexane extract and methanol extract were 84.37% and 66.79% respectively (39).

4.4.8. Anthelmintic activity

The anthelmintic efficacy of fruit extracts from *Melia azedarach* plants was examined in a study by Szewczuk et al. published in 2006. The extracts were tested against the hookworm "*Bunostomum trigonocephalum*", the nodular worm "*Oesophagostomum columbianum*", the tapeworm "*Taenia solium*", and the earthworm "*Pheretima*

posthuma". Hexylresorcinol and piperazine phosphate were utilized as comparison examples. Table 2 shows the classification of worms and diseases they cause.

Table 3. The classification of worms and diseases they cause

Scientific name	Group	Common name	Host	Disease
<i>Taenia solium</i>	Cestoda	Pork tapeworm	Pig, man	Taeniasis (adult form and cysticercosis (larval form))
<i>Bunostomum trigonocephalum</i>	Nematoda	Sheep hookworm	Sheep, goats	Gastrointestinal infection
<i>Oesophagostomum columbianum</i>	Nematoda	Nodular worm	Sheep, goats	Gastrointestinal infection
<i>Pheretima posthuma</i>	Annelida	Earthworm	Sheep, goats	Gastrointestinal infection

The results indicated that *Melia azedarach* fruit exhibited higher activity against hookworms and tapeworms compared to piperazine phosphate and hexylresorcinol, respectively. However, the lethal effect on nodular worms was lower than that of hexylresorcinol. The mean time of death values for the drupe extract of *Melia azedarach* against tapeworms (52 minutes at 0.1% concentration and 32 minutes at 0.2% concentration) were superior to those observed for hexylresorcinol (38 and 20 minutes) (40).

In a study conducted by Cala et al. in 2012, the in vitro anthelmintic effects of fruit extracts obtained from *Melia azedarach* were evaluated against sheep gastrointestinal nematodes using the egg hatch test (EHT) and larval development test (LDT). The hexane extract exhibited anthelmintic activity (41).

In a previous study, Gajmer et al. (2002) conducted research to evaluate the anthelmintic activity of *Azadirachta indica* and *Melia azedarach* seeds collected from

India. The study involved extracting the seeds of both *A. indica* and *Melia azedarach*, which belong to the Meliaceae family, using methanol. Subsequently, the effects of these seed extracts from *Azadirachta indica* and *Melia azedarach*, respectively, were examined on the oviposition and egg hatching of *Earias vittella*, an Asian "spotted bollworm" known for attacking the fruiting bodies of certain crops, particularly cotton. The results of the study indicated that the methanolic extracts obtained from *Azadirachta indica* and *Melia azedarach* showed adverse effects on the egg-laying behavior, fecundity, and hatching of *E. vittella* eggs. Specifically, the extracts derived from *Azadirachta indica* seeds exhibited more pronounced effects compared to the extracts from *Melia azedarach* seeds (42).

4.4.9. Wound healing activity

In a study published in 2012, Vidya et al. conducted an investigation to assess the wound healing properties of *Melia azedarach* leaf extract in alloxan-induced diabetic rats. The evaluation of wound healing efficacy was performed using an excision wound model, with povidone iodine ointment serving as the reference standard. The study measured and analyzed wound contraction and the percentage of wound contraction for a duration of 18 days. The leaves of *Melia azedarach* were collected from India and subjected to methanol extraction.

The findings demonstrated that the topical application of methanolic *Melia azedarach* leaf extract promoted wound healing in diabetic rats, with a comparable effect to the standard povidone iodine. The enhanced wound healing observed in diabetic rats could be attributed to the antimicrobial activity of the *Melia azedarach* leaf extract (43).

In a study published in 2015, Kumar et al. conducted research to assess the wound healing properties of *Melia azedarach* leaf ethanolic extract in rats. The study utilized both the excision and incision wound healing models, with povidone-iodine serving as the standard drug. The evaluation of wound healing efficacy involved measuring wound contraction, epithelization time in the excision wound model, and tensile strength in the incision wound model over a period of 16 days.

The findings revealed that the topical application of ethanolic *Melia azedarach* leaf extract at different concentrations (5% and 10%) exhibited a significant effect in

reducing the wound area and epithelization time in the excision wound model. Furthermore, the extract demonstrated a notable effect on tensile strength in the incision wound model. The wound healing activity of the extract was found to be significantly higher compared to the standard treatment (44).

In a study published in 2015, Al-Khafaji et al. conducted a performance evaluation of *Melia azedarach* fruit ointment in the surgical wound healing process in donkeys, comparing it to natural wound healing without any medication. The evaluation encompassed both clinical and histopathological examinations. Incisions measuring 10-12 cm in length were bilaterally created in the thigh and neck regions of donkeys aged 4-5 years. The wounds were treated daily with a 10% *Melia azedarach* fruit ointment for duration of 14 days. Biopsies were obtained from the wounds on day 5, 10, and 15 for histopathological examination.

The findings demonstrated that *Melia azedarach* exhibits anti-inflammatory and antibacterial activities. The fruit ointment proved effective in treating infected wounds, leading to clinical and histopathological healing within a 15-day timeframe (45).

4.4.10. Anticancer activity

In a study published in 2020, by Nerome et al. conducted an investigation to evaluate the anticancer effects of *Melia azedarach* aqueous leaf extracts against HT-29 colon”, “A549 lung”, and “MKN1 gastric cancer cell lines. The results revealed that the extracts of *M. azedarach* exhibited potent antiproliferative activity against HT-29, A549, and MKN1 cancer cell lines in the colon, lung, and stomach, respectively. Furthermore, in mice with transplanted MKN1 gastric cancer xenografts, significant growth inhibition was observed upon treatment with *Melia azedarach* leaf extracts. Similarly, in veterinary hospitals, dogs suffering from different malignancies showed an average recovery rate of 76% when administered *Melia azedarach* leaf extracts. This study also identified that the *Melia azedarach* leaf extract acts as an autophagy-inducing agent and stimulates the production of Tumor Necrosis Factor-alpha (TNF- α), which may play a role in inhibiting in vivo tumor growth (46).

In a study published in 2013, Jafari et al. conducted research to evaluate the anticancer properties of *M. azedarach* leaves, seeds, and fruits extracts on HT-29, "A-549", "MCF-7", "HepG-2", and "MDBK" cell lines. The results indicated that *M. azedarach* seed extract exhibited the highest level of cytotoxicity and selectivity against these cancer cell lines, with an IC₅₀ range of 8.18–60.10 µg/mL. On the other hand, *M. azedarach* leaf methanol extract showed a relatively lower cytotoxic effect (47).

In a study published in 2023, by Satia et al. conducted research to assess the anticancer effect of *M. azedarach* methanolic leaf extract against LNCaP, MDAMB-231, and MCF-7 cancer cell lines. The results revealed that the extract exhibited low to moderate anticancer activity against LNCaP, MDA-MB-231, and MCF-7 cell lines. In this study anticancer activity of *M. azedarach* attributed to kaempferol 7-O-rutinoside 1 and 4-methoxyresorcinol (48).

In an another study published in 2021, by Shyam et al. evaluated the anticancer effect of *M. azedarach* leaf extract against human ovarian and human pancreatic cancer cells by using the 3-(4,5- dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide) assay (MTT). The results revealed that the extract exhibited moderate anticancer activity where the IC₅₀ was less than 50 µg/mL on pancreatic cancer cell lines while on human ovarian cancer cells IC₅₀ was 26.4 µg/mL (49).

In a study published in 2022, by Song et al. to assess the anticancer effect of triterpenoids were isolated from the fruits of *M. azedarach* against HCT116, RKO, A549, BEL7402, and MCF-7 cancer cell lines. The results revealed that the anticancer activity against five cancer cell lines with IC₅₀ values ranging from 9.02 to 31.31 µM (50).

4.4.11. Analgesic and antipyretic activities

In a study published in 2016, Vekariya et al. conducted research to evaluate the analgesic and antipyretic activities of *Melia azedarach* leaves and roots collected from India. The analgesic effects were assessed using the acetic acid-induced writhing test in mice and the radiant heat-induced pain test in albino rats, while the antipyretic activity was evaluated against Brewer's yeast-induced pyrexia in Charles Foster rats.

The findings of the study revealed that *Melia azedarach* roots exhibited minimal to moderate effects on both peripheral and central analgesia. However, no discernible

analgesic activity was observed with *Melia azedarach* leaves in either of the experimental models. Furthermore, the roots of *Melia azedarach* significantly reduced rectal temperature after 3 to 6 hours, whereas the leaves showed a temperature reduction after 6 hours. Based on these results, it can be concluded that the roots of *Melia azedarach* possess a more pronounced antipyretic effect compared to the leaves of *Melia azedarach* (51).

In a study published in 2013, Sultana et al. conducted research to assess the antipyretic effect of *Melia azedarach* leaves collected from Pakistan. The leaves were extracted with methanol through a 72-hour maceration process. The antipyretic effect of the hydro-methanol extract of *M. azedarach* leaves was investigated using the yeast-induced pyrexia method in rabbits, with paracetamol used as the reference drug. Rectal temperatures of the rabbits were recorded before administration of the extract, vehicle, or paracetamol, and subsequently at one-hour intervals for duration of six hours using a digital thermometer.

The results indicated that the 500 mg/kg dose of the extract exhibited a significant decrease in temperature caused by yeast, comparable to the effects of the commonly used medication, paracetamol. However, the 250 mg/kg dose of the extract showed less effectiveness compared to higher doses. Therefore, it can be concluded that the hydro-methanol extract of *M. azedarach* leaves, at a dose of 500 mg/kg, possesses a significant antipyretic effect against yeast-induced elevated temperature (52).

In a study published in 2013, Asadujjaman et al. conducted research to assess the analgesic effect of *Melia azedarach* leaves collected from Bangladesh. The leaves were extracted with ethanol through a 15-day maceration process. The analgesic effect of the ethanolic extract from *Melia azedarach* leaves was investigated using the acetic acid-induced writhing test in mice. As a reference drug, diclofenac sodium was administered at a dose of 25 mg/kg body weight.

The findings demonstrated that the ethanolic extract of *Melia azedarach* leaves exhibited dose-dependent writhing inhibition. At doses of 250 and 500 mg/kg, the extract showed writhing inhibition rates of 45.45% and 67.05% respectively. These results were comparable to the standard diclofenac sodium, which exhibited a writhing inhibition rate of 69.32% at a dose of 25 mg/kg (53).

4.4.12. Toxicity

To assess the toxicity of *Melia azedarach* flowers and berries, experiments were performed on rats and mice using both water and alcohol extracts. The administration routes included oral ingestion and intravenous injection. The findings revealed that the water and alcohol extracts exhibited no toxicity up to a dose of 1500 mg/kilogram when administered orally to mice and rats. Intravenous injection of the aqueous extract resulted in LD₅₀ values of 395 mg/kg in mice and 500 mg/kilogram in rats for flowers, while berries showed LD₅₀ values of 700 mg/kg in mice and 925 mg/kg in rats (54). Another study to determine LD₅₀ orally and intraperitoneally of *Melia azedarach* fruit extracts on rats. The result was that oral administration of a maximum of 16 g/kg of extract did not cause major behavioral changes, morbidity or mortality in rat. Nevertheless, the intra-peritoneal LD₅₀ was 1.03 g/kg. The lung was the directly impacted organ in the intraperitoneal research according to histopathology, which also revealed muscle disintegration, a significant inflammatory infiltration surrounding the bronchi and bronchioles, and an increase in the mucous production of the epithelial cells that line the bronchi (55). Toxicity not depends only on dose but also on the part plant used and route of administration. A higher extract concentration significantly slows down breathing (55).

4.5. Some products in market, containing *Melia azedarach*

Extracts and derivatives of *Melia azedarach* have been incorporated into various products for their potential benefits. Table 4 shows some examples

Table 4. Some products containing *Melia azedarach*

Name of product	Photo	Dosage form	Electronic literature
LOCPILES		Capsule	https://www.piousayurveda.com/locpiles-capsules.html
Neeri KFT		Syrup	https://healthplus.flipkart.com/neeri-kft-sugar-free-syrup-200-ml-aimil-pharmaceuticals-india-ltd-h/p/vdmhz2
Beplate		Syrup	https://www.indiamart.com/roddetail/beplate-200ml-syrup-23223528673.html
Carpago Forte		tablet	https://www.alna.in/product/alna-carpago-forte-tab-10x10-tablets

Pylno		Cream	https://www.ayurvedicherbalsindia.com/herbal-piles-cream.html
Neem seed oil		Oil	https://www.ciceksepeti.com/arifoglu-tesbih-agaci-yagi-20-ml-kcm58690463
Pill Heal		Capsules	https://www.indiamart.com/proddetail/pill-heal-herbal-piles-capsules-13635779997.htm

5. DISCUSSION AND CONCLUSION

The comprehensive key findings from the literature review provide valuable insights into the biological activities, chemical composition of *Melia azedarach*, and its importance in phytotherapy. According to the literature review, *Melia azedarach* has a lot of pharmacological activities, such as “antibacterial”, “anti-inflammatory”, “anthelmintic,” “antioxidant”, “antitumor”, “analgesic”, and “antipyretic activities”.

One of the prominent biological activities observed in *Melia azedarach* is its antibacterial and antifungal properties. Several studies have demonstrated the plant's ability to inhibit the growth of various bacterial strains and fungus, this activities attributed to Limonoids such as “azadirachtin”, “gedunin”, “scopolotin” and “meliacarpin”, indicating its potential as a natural antimicrobial agent. This finding holds significant importance in the field of phytotherapy, as the rise of antibiotic resistance necessitates the exploration of alternative treatment options (20-23).

Furthermore, the studies have shown the ability of *Melia azedarach* to inhibit the replication of various viral pathogens, this activity attributed to “meliacine” compound suggesting its possible application in the development of antiviral therapies (24-25).

Furthermore, the antiparasitic activity of *Melia azedarach* which including “antileishmanial activity” “antimalarial activity” and “anthelmintic activity” is attributable to limonoids compound (26-29, 40-42).

Regarding to “anti-inflammatory effects” *Melia azedarach* has exhibited “anti-inflammatory effects”. Inflammation is involved in the pathogenesis of various diseases, and the plant's extracts have demonstrated the ability to reduce inflammation through the inhibition of pro-inflammatory mediator which include prostaglandin and cytokines, and pro-inflammatory enzymes which include cyclooxygenases and lipoxygenases which are responsible for promoting inflammation. (32-35).

Another notable biological activity of *Melia azedarach* is its “antioxidant” capacity. Oxidative stress plays a crucial role in various diseases, including cardiovascular disorders, neurodegenerative conditions, Alzheimer and cancer. The *Melia azedarach* as demonstrated in several studies, ability to scavenge free radicals and reduce oxidative

stress. Thus potentially contributing to the prevention or management of various diseases associated with oxidative stress. Studies indicate that this activity of *M. azedarach* is thanks to its possession of phenolic compounds (26, 36-39).

Additionally, *Melia azedarach* has shown promising “wound healing activity”. Studies have indicated its ability to promote the healing of wounds, including its effects on cellular proliferation, collagen synthesis, and angiogenesis. These properties make it a potential candidate for the development of wound healing agents and formulations (43-45).

Moreover, the evaluation has indicated potential “anticancer properties” of *Melia azedarach*. Studies have shown its ability to inhibit the growth and proliferation of cancer cells. The plant's bioactive compounds, such as “flavonoids” and “limonoids”, have been implicated in exerting cytotoxic effects on cancer cells and disrupting cancer progression. These findings hold promise for the development of novel therapeutic strategies in cancer treatment (46-50).

The *Melia azedarach* plant extracts have shown the potential to alleviate pain and reduce fever. These effects are particularly valuable in the management of pain-related conditions and fever associated with various infections (51-53).

In conclusion, these findings from the literature review provide robust evidence supporting the diverse biological activities of *Melia azedarach*. Its antimicrobial, antifungal, anti-inflammatory, and potential anticancer properties make it an intriguing candidate for further exploration in phytotherapy. However, additional investigation is required to clarify the exact mechanisms through which it operates, identify the active compounds responsible for these activities, and evaluate their safety and efficacy in clinical settings. The wealth of evidence accumulated through these studies underscores the importance of *Melia azedarach* as a valuable resource in the field of phytotherapy, prompting further investigation into its therapeutic potential.

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THE FIRST PAGE OF PLAGIARISM REPORT

EVALUATION OF BIOLOGICAL ACTIVITIES OF MELIA AZEDARACH SPECIES AND ITS IMPORTANCE IN PHYTOTHERAPY

ORJİNALLİK RAPORU

% 17	% 13	% 10	% 5
BENZERLİK ENDEKSİ	İNTERNET KAYNAKLARI	YAYINLAR	ÖĞRENCİ ÖDEVLERİ

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