Toxicology Reports 14 (2025) 101900

Contents lists available at ScienceDirect

Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

Recent developments on ursolic acid and its potential biological applications

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ARTICLE INFO

Keywords:
Metabolic Health
Antimicrobial
Neuroprotective
Hyperlipidaemia
Ursolic acid

ABSTRACT

A naturally occurring pentacyclic triterpenoid, ursolic acid (UA) has attracted a lot of interest due to its various pharmacological characteristics and its medical uses. The goal of this thorough review is to present a thorough examination of the therapeutic benefits of UA, including its anti-inflammatory, antioxidant, anticancer, antibacterial, and metabolic-regulating properties. We go over its origins, pharmacological characteristics, and advantages in the treatment of several illnesses, including cancer, neurological disorders, metabolic disorders, and cardiovascular diseases. We further emphasize its potential to improve exercise capacity and its growing function as an exercise mimic. UA's therapeutic potential is thoroughly explained in this review, which highlights the compound's potential as a natural remedy for several illnesses.

1. Introduction

Ursolic acid (UA) (3β-hydroxy-urs-12-en-28-oic-acid) a naturally occurring triterpenoid compound found in plants such as apple peel, rosemary, marjoram, and oregano, has attracted significant attention due to its diverse biological activities and potential therapeutic applications [1]. Known for its anti-inflammatory, antioxidant, anticancer, and metabolic-regulating effects, UA (Fig. 1) exists both in its free form and as saponins, bound to sugar chains. Structurally similar to steroids, UA is synthesized from squalene, a key precursor, underscoring its importance in plant secondary metabolism and potential benefits for human health [2].

UA's special capacity to control several important biochemical pathways accounts for its medicinal promise. For example, it has been demonstrated to reduce inflammation and related illnesses by modifying inflammatory signaling cascades, including cyclooxygenase-2 (COX-2), mitogen-activated protein kinase (MAPK), and nuclear factor kappa B (NF-κB). Furthermore, by scavenging free radicals and boosting the activity of endogenous antioxidant enzymes like catalase (CAT) and superoxide dismutase (SOD), UA has a significant impact on oxidative stress [3]. Its effectiveness in treating conditions including cancer, neurological diseases, and cardiovascular diseases marked by oxidative damage and chronic inflammation is supported by its combined anti-inflammatory and antioxidant properties [4].

The use of UA in the prevention and treatment of cancer is among its most promising uses. Breast, prostate, liver, and colorectal malignancies are among the many cancer types for which UA has shown strong anticancer benefits. Its capacity to limit tumor cell growth and metastasis, block angiogenesis, and induce apoptosis is responsible for these actions [5]. Mechanistically, UA targets several biological pathways that contribute to the development of cancer, including Wnt/β-catenin signaling, phosphatidylinositol-3-kinase/protein kinase B (PI3K/Akt), and mammalian target of rapamycin (mTOR). Additionally, it has been demonstrated that UA increases the effectiveness of traditional chemotherapeutic medicines, suggesting that it could be used as an adjuvant therapy to improve the results of cancer treatment [6].

In metabolic health, UA has shown promise in the fight against diabetes, obesity, and other metabolic diseases. One of the main risk factors for the onset of type 2 diabetes and cardiovascular disorders is obesity, which is defined by insulin resistance and persistent low-grade

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https://doi.org/10.1016/j.toxrep.2025.101900
Received 17 October 2024; Received in revised form 25 December 2024; Accepted 6 January 2025
Available online 10 January 2025

inflammation. UA's anti-obesity and anti-diabetic properties are a result of its capacity to control the insulin signaling pathways, adipogenesis, and lipolysis [7]. In animal models of metabolic diseases, research has shown that UA can decrease lipid buildup, increase insulin sensitivity, and improve glucose homeostasis. Additionally, UA's ability to activate AMP-activated protein kinase (AMPK) further underscores its potential in managing metabolic dysregulation and associated complications [8].

Significant attention has also been paid to UA's neuroprotective qualities, especially to neurodegenerative illnesses like Parkinson's disease (PD) and Alzheimer's disease (AD). These disorders are characterized by chronic neuroinflammation, oxidative stress, and neuronal apoptosis [9]. UA's ability to attenuate oxidative damage, reduce neuroinflammation, and enhance neuronal survival positions it as a promising therapeutic agent for mitigating neurodegeneration. In preclinical studies, UA has been shown to improve cognitive function, reduce amyloid-β plaque deposition, and inhibit the activation of microglia and astrocytes—key mediators of neuroinflammation—in animal models of AD. These findings highlight the potential of UA to slow the progression of neurodegenerative diseases and improve the quality of life for affected individuals [10].

Numerous studies have demonstrated UA's hepatoprotective properties, which include reducing liver damage brought on by pollutants, alcohol, and metabolic diseases. With few available treatments, liver illnesses such as alcoholic liver disease (ALD), hepatic fibrosis, and non-alcoholic fatty liver disease (NAFLD) are serious worldwide health issues. It has been demonstrated that UA significantly alleviates oxidative stress, inflammation, and fat buildup in the liver [11,12]. Its promise as a treatment for chronic liver illnesses is further highlighted by its anti-fibrotic qualities, which are mediated by the prevention of hepatic stellate cell activation and extracellular matrix deposition [13].

An intriguing aspect of UA's pharmacological profile is its potential to act as an exercise mimetic, enhancing muscle performance and preventing muscle atrophy. Muscle atrophy, a common consequence of aging, chronic diseases, and physical inactivity, poses significant health risks, including metabolic dysfunction and increased morbidity [14]. UA has been shown to upregulate key pathways involved in muscle protein synthesis, such as the insulin-like growth factor-1 (IGF-1)/Akt signaling axis, while simultaneously downregulating pathways associated with muscle protein degradation, such as the ubiquitin-proteasome system. These effects not only improve muscle mass and strength but also enhance overall metabolic health, making UA a promising candidate for addressing sarcopenia and other muscle-wasting conditions [15].

Although UA has a wide range of therapeutic possibilities, there are several obstacles to its clinical application. Its low solubility and quick metabolism in the liver and gastrointestinal system are the main causes of its poor bioavailability. Numerous approaches have been investigated to get over these obstacles, such as creating liposomes, UA-loaded nanoparticles, and other innovative drug delivery methods [16]. Furthermore, UA's pharmacokinetic profile and therapeutic efficacy have been improved through chemical changes. These developments in the formulation and distribution of UA have the potential to enhance its therapeutic results and clinical usability.

A crucial component of UA research is the requirement for economical and sustainable production techniques. To address the increasing demand for UA-based medicines, UA is now mostly taken from plant sources, which might not be enough. Potential remedies for scalable and sustainable UA production are provided by biotechnological techniques including metabolic engineering and microbial fermentation. Furthermore, the effective manufacture of UA and its derivatives may be made possible by developments in synthetic biology and organic synthesis, guaranteeing its accessibility for use in clinical and industrial settings [17,18].

Moreover, UA represents a promising natural compound with a wide range of therapeutic applications. Its ability to modulate key biological processes, such as inflammation, oxidative stress, apoptosis, and metabolic regulation, underscores its potential for addressing chronic diseases, including cancer, neurodegenerative disorders, metabolic conditions, and liver diseases [19]. Moreover, its emerging role as an exercise mimetic highlights its potential to improve muscle health and metabolic fitness in aging populations and individuals with chronic illnesses. While significant progress has been made in understanding UA's pharmacological properties, further research is needed to overcome challenges related to its bioavailability, production, and clinical translation [20].

In the twenty-first century, UA has the potential to become a key component of natural product-based therapies by tackling these issues and utilizing developments in biotechnology and drug delivery. To ensure its accessibility and use in clinical settings, this study intends to present a thorough analysis of UA's therapeutic effects, with an emphasis on liver diseases, neurological disorders, metabolic conditions, and its potential as an exercise mimic. It also emphasizes the necessity of sustainable production strategies.

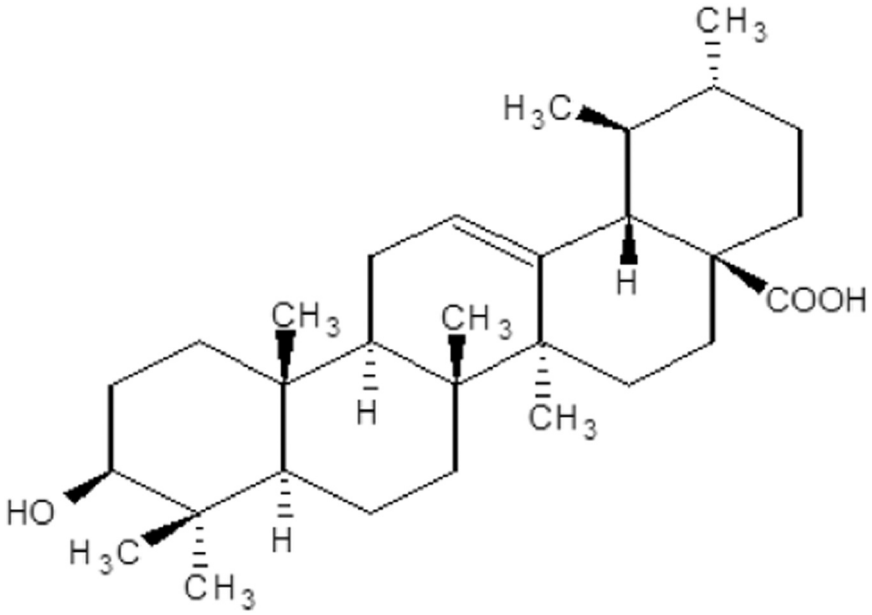

Fig. 1. Structure of UA ($C_{30}H_{48}O_3$).

2. Occurrence of UA in folk medicine

Plants high in UA have a long history of use in traditional medicine, where they have been valued for their diverse therapeutic properties, including hepatoprotective, pain-relieving, cardio-tonic, relaxing, and tonic effects. These plants have been used to treat a variety of ailments, such as liver disorders, cardiovascular issues, and inflammation, and have been recognized for their general restorative qualities [21]. Over time, modern scientific research has provided validation for many of these traditional uses, confirming the beneficial effects of UA and its potential for treating a range of health conditions. Studies have demonstrated its ability to protect the liver from damage, reduce pain, enhance heart function, and provide overall health benefits, reinforcing its therapeutic potential in modern medicine (Table 1).

3. Sources of UA

UA is a triterpenoid compound that is found in a wide range of plants, fruits, and medicinal herbs, contributing to their therapeutic properties. It is prevalent in plants such as Melissa *officinalis* (lemon balm) [35], Piper betle (betel leaf) [36] Rosemary (*Rosmarinus officinalis L.)* [37], and other plants. Fig. 2, Fig. 3, and Fig. 4 show the *Melissa officinalis* (lemon balm), Piper betle (betel leaf), and Rosemary (*Rosmarinus officinalis L.)*, respectively. The compound is also present in the protective waxy coatings of various fruits, including apples, pears, cranberries, and prunes, as well as in certain species of seaweed. These natural sources make UA, a valuable compound with a broad spectrum of potential health benefits, including anti-inflammatory, antioxidant, and anti-cancer properties. Its widespread occurrence in both common foods and traditional medicinal plants underscores its importance in both diet and herbal medicine.

3.1. Lemon balm

Melissa officinalis Commonly known as lemon balm, is an evergreen herbaceous plant from the mint family (Lamiaceae). Typically reaching 50 cm in both height and width, lemon balm is easily recognizable by its lemon-scented crushed leaves, which are often described as having a pleasant, citrus-like fragrance. It is also known by various other names, including balm, bee balm, garden balm, and balm mint [37,38]. This hardy plant thrives in many habitats, including waste areas, neglected terrains, forests, sunny edges, dappled shade, and shady spots, often growing near human settlements. Originally native to Southern Europe, particularly in the hilly regions, lemon balm has since naturalized in several countries, including England, Hungary, Iraq, Panama, Spain, Turkey, and the United States. Due to its adaptability and aromatic properties, it has become a popular plant for culinary use and traditional medicine. The leaves of *Melissa officinalis* are widely appreciated for their pleasant lemon-like scent and flavor. They are often added to salads and cooked dishes to impart a fresh, citrusy taste [39]. Both fresh and dried leaves are commonly used to prepare lemon-flavored tea, which can be enjoyed on its own or blended with other types of tea, such as China tea, to enhance its flavor. In addition to its use in teas, lemon balm leaves are also used to flavor fruit cups, desserts, and a variety of culinary dishes. Furthermore, the leaves find their way into the production of alcoholic beverages, such as the herbal liqueurs Chartreuse and Benedictine, where they contribute to the distinctive flavors of these drinks.

The medicinal use of *Melissa officinalis* has a long history, dating back to ancient times. It was first recorded in the "Materia Medica" around 50–80 AD. By the Middle Ages, lemon balm was widely used throughout Europe for its therapeutic properties. Renowned figures such as Paracelsus (1493–1541) championed its use, particularly for its rejuvenating effects. Paracelsus believed that lemon balm could "completely revivify a man" and recommended it for treating ailments believed to stem from a disordered nervous system [40]. During this period, herbal apothecaries also linked lemon balm tea to improvements in cognitive function,

Table 1
A short overview of beneficial plants with UA as an active component.

S. No	Name of the plant	Family	Biological activity	Reference
1	*Sambucus chinesis*	Caprifoliaceae	Hepatoprotection	[22]
2	*Solanum incanum*	Solanaceae	Hepatoprotection	[23]
3	*Tripterospermum taiwanese*	Gentianaceae	Hepatoprotection	[24]
4	*Eucalyptus hybrid*	Myrtaceae	Hepatoprotection	[25]
5	*Calluna vulgaris*	Ericaceae	Inhibiting lipoxygenase and cyclooxygenase in human leukemia HL−60 cells	[26]
6	*Eriobotrya japonica*	Rosaceae	Inhibition of lipoxygenase in bacteria	[27]
7	*Glechoma hederacea*	Lamiaceae	Antitumor promotion	[28]
8	*Melaleuca leucadendra*	Myrtaceae	Reduction of histamine output	[29]
9	*Ocimum sanctum*	Lamiaceae	Reduction of lipid peroxidation, protection against Adriamycin toxicity, antimicrobial activity	[30]
10	*Rosmarinus officinalis*	Lamiaceae	Antimicrobial activity, suppression of mouse skin tumorigenesis	[31,32]
11	*Pyrola rotund folia*	Prolicide	Anti-inflammation	[33]
12	*Psychotria serpens*	Rubiaceae	Cytotoxic to leukemia cells	[34]

Fig. 2. *Melissa officinalis* leaves [35].

Fig. 3. Piper betle [36].

Fig. 4. Rosemary [37].

including memory enhancement. This historical usage highlights the herb's long-standing reputation for promoting overall well-being, particularly mental and emotional health. *Melissa officinalis* has a well-established safety profile with no harmful side effects reported in its typical uses. To date, there have been no indications of toxicity, and studies have shown that it exhibits no genotoxicity *in vitro*, meaning it does not cause genetic damage or mutations. This reinforces its reputation as a safe and beneficial herb when used appropriately [41].

Melissa officinalis possesses a diverse range of pharmacological properties, making it a valuable herb in both traditional and modern medicine. Among its many effects, lemon balm is known for its antibacterial, antiviral, and antispasmodic properties, which help relieve muscle spasms. It also serves as a carminative, alleviating flatulence and digestive discomfort, and as a diaphoretic, promoting perspiration to aid in fever reduction. Additionally, lemon balm is used in aromatherapy for pain control via its essential oils, and its sedative and anti-anxiety effects help to alleviate agitation and stress [42]. The herb also has beneficial effects on the digestive system and is considered an emmenagogue (promotes menstruation) and a febrifuge (reduces fever). Modern research has further expanded our understanding of its therapeutic potential, demonstrating its hepatoprotective properties, which help protect the liver, as well as its antioxidant, antiperoxidative, and antistress effects. Lemon balm has also shown promise in antitumoral, antimicrobial, anti-HIV-1, and anti-herpes activity, highlighting its broad spectrum of action against various pathogens and diseases. Moreover, it has been found to improve cognitive function and mood, making it useful in the treatment of mild to moderate Alzheimer's disease, where it may help with cognitive decline and overall mental well-being [43].

3.2. Betel leaf

The perennial vine *Piper belt*, referred to as betel leaf, belongs to the Piperaceae family [44]. Known for its glossy, heart-shaped leaves and unique scent, this evergreen plant grows well in tropical and subtropical climates. In South and Southeast Asia, betel leaf is highly valued in culture and is utilized extensively in religious ceremonies, traditional medicine, and culinary preparations. Because it climbs, it is grown on trellises and thrives in warm, humid areas. Because of its adaptability and versatility, it has become a vital component of many communities' customs and health practices [45].

Betel leaves are prized for their strong, slightly sweet taste and are an essential component of the traditional dish "paan." This involves wrapping the leaves in a mixture of slaked lime, areca nuts, and other spices or sugars. In addition to this cultural custom, betel leaves are used in teas, herbal medicines, and cuisine to improve flavor. These leaves are a mainstay in traditional medical systems like Ayurveda, Unani, and Siddha because of their abundance of medicinal chemicals. They have been used for ages to cure skin infections, stomach disorders, and respiratory problems. Their use as digestion aids, oral hygiene products, and poultices demonstrates their many therapeutic applications. [46].

Numerous traditional statements of Piper betle have been validated by contemporary research, demonstrating its wide range of pharmacological characteristics. Betel leaves are efficient against infections like Staphylococcus aureus, Escherichia coli, and Candida albicans because of their potent antibacterial, antifungal, and antiviral properties. These antibacterial qualities are especially beneficial for wound treatment, infection prevention, and dental hygiene. Additionally, the anti-inflammatory and analgesic properties of betel leaves help reduce pain and swelling, with poultices often used for localized injuries and inflammatory conditions [47].

The digestive advantages of betel leaves are also well-known. They relieve indigestion, gas, and bloating by acting as stomachic and carminatives. Chewing betel leaves stimulates the secretion of digestive enzymes, improving gastrointestinal function. Studies demonstrating their hepatoprotective benefits have shown protection against oxidative stress and toxin-induced liver damage. Additionally, their antioxidant qualities aid in the defense against free radicals, lowering the incidence of long-term illnesses like cancer, heart disease, and neurological problems [48].

The Piper betle's neuroprotective properties are very remarkable. According to research, its bioactive components may reduce the incidence of Parkinson's and Alzheimer's illnesses by shielding neurons from inflammation and oxidative stress. The traditional usage of betel leaves to lower stress and increase alertness may be explained by their anxiolytic and mood-enhancing properties. Betel leaves have also been proven to have antihypertensive and vasodilatory properties, which support cardiovascular health. By enhancing insulin sensitivity and controlling blood glucose levels, they also demonstrate antidiabetic

qualities [49].

When taken naturally and sparingly, Piper betle has a good safety record. However, it is important to distinguish the medicinal advantages of betel leaves from the negative effects of betel quid (paan) which contain tobacco and areca nut. To further confirm its efficacy and safety, future studies should concentrate on improving the bioavailability of its active ingredients, creating standardized formulations, and carrying out clinical trials [50]. In conclusion, Piper betle is a multipurpose medicinal herb that has been validated by science and has a long history of traditional use. It is a useful natural therapy because of its antibacterial, anti-inflammatory, antioxidant, and neuroprotective qualities. Betel leaves have great potential for modern medicine while maintaining their cultural and therapeutic heritage with sustainable farming and ongoing research.

3.3. Rosemary

The aromatic plant *Rosmarinus officinalis L.* (Syn. *Salvia rosmarinus Spenn.*), commonly referred to as rosemary, is a member of the Lamiaceae family and has needle-like leaves. Commonly referred to as rosemary, *Rosmarinus officinalis L.* is an aromatic evergreen shrub that is a member of the Lamiaceae family [51]. It is native to the Mediterranean region and is grown extensively for its fragrant, culinary, and medicinal qualities. Known for its woody scent and needle-like leaves, rosemary grows best in sunny, well-drained conditions and is now a common herb in gardens and herbal medicine all over the world.

Because of its therapeutic and symbolic meaning, rosemary has long been valued. It was frequently utilized in ceremonies and rituals in ancient Greece and Rome as a symbol of loyalty and remembering. Rosemary leaves and essential oils have long been used in traditional medical systems to treat a variety of illnesses, such as skin, respiratory, and digestive disorders. It was also praised for improving mental clarity and memory [52].

Rosemary has many culinary applications, and its strong, slightly bitter flavor makes it a common flavoring for baked items, meats, and vegetables. Additionally, it is utilized in marinades, infused oils, and herbal drinks. Beyond its ability to enhance flavor, rosemary is a crucial component of functional meals because of its bioactive components, which also add to its health advantages. Numerous traditional statements on the therapeutic benefits of rosemary have been confirmed by contemporary scientific research. Flavonoids, polyphenols (such as rosmarinic acid, and caffeic acid), and essential oils (including 1,8-cineole, camphor, and α-pinene) are abundant in it. These substances give rosemary strong antibacterial, anti-inflammatory, antioxidant, and neuroprotective properties [53].

The antioxidant activity of rosemary, which aids in scavenging free radicals and lowering oxidative stress, is among its most important advantages. A decreased risk of chronic illnesses like cancer, heart disease, and neurological problems is associated with this protective impact. Because of its anti-inflammatory qualities, which are mostly ascribed to rosmarinic acid, rosemary is useful in the treatment of inflammatory diseases like arthritis. Particularly remarkable are rosemary's neuroprotective properties. Its active ingredients have been shown to strengthen cognitive function, enhance mental clarity, and improve memory. Rosemary essential oil is effective in aromatherapy since it has been demonstrated to lower stress and anxiety. By reducing inflammation and oxidative stress in neurons, it may also help prevent or halt the progression of neurodegenerative illnesses like Alzheimer's [54].

Because of its antibacterial qualities, which work against bacteria, fungi, and viruses, rosemary is a good addition to cosmetics and oral hygiene products as well as a natural food preservative. Additionally, its antimicrobial properties aid in the fight against infections and support the general health of the skin. Additionally, rosemary alleviates indigestion, flatulence, and bloating by acting as a stomachic and carminative. Further improving liver function and preventing liver damage are its hepatoprotective qualities. Although rosemary has a wide range of therapeutic uses, excessive dosages should be used with caution as concentrated essential oil might have negative side effects like allergic responses or gastrointestinal distress. Because of the possible hazards, pregnant and lactating women should avoid excessive doses of rosemary. Nonetheless, rosemary is often safe and quite helpful in the right amounts [55].

As a result, Rosmarinus officinalis L. is a multipurpose herb with a long history and a wide range of health advantages. It is a vital natural therapy because of its antibacterial, neuroprotective, anti-inflammatory, and antioxidant qualities. Rosemary continues to be a useful tool in aromatherapy, culinary arts, and both conventional and modern medicine as studies into its possibilities continue.

3.4. Apples

Apples (*Malus domestica*) are one of the world's most frequently farmed and consumed fruits, belonging to the Rosaceae family. They are not only delicious, but also adaptable since they can be eaten fresh, dried, juiced, or cooked into a variety of cuisines including pies, sauces, and desserts. The fruit holds considerable cultural and symbolic value in a variety of traditions, including Western mythology, where it represents wisdom and temptation [56].

Apples are nutrient-dense, containing dietary fiber, vitamin C, and a variety of polyphenolic chemicals that have been associated with several health benefits. These chemicals include flavonoids and phenolic acids, which help to boost their antioxidant activity. Regular consumption of apples has been associated with reduced risks of cardiovascular diseases, improved gut health, and better regulation of blood sugar levels. Additionally, apple peels contain quercetin, a potent antioxidant and anti-inflammatory agent. Studies have also suggested that apples may play a role in weight management and the prevention of certain cancers.

UA is a naturally occurring triterpenoid found primarily in apple peel (*Malus domestica*). The concentration of UA in apple peels varies between 40 and 90 mg per 100 g, depending on the variety, growth conditions, and fruit ripeness. The flesh of apples contains substantially less, hence the peel is the principal source of extraction. Apples, particularly their peels, have a high concentration of UA, a bioactive chemical with numerous therapeutic applications. Its inclusion in functional foods, dietary supplements, and medications has the potential to treat a wide range of health issues, including chronic inflammation, metabolic problems, skin aging, and neurodegenerative illnesses [57].

3.5. Bilberries

Bilberries (*Vaccinium myrtillus*), often called European blueberries, are small, dark blue berries that grow on low shrubs in the Ericaceae family. Bilberries are native to Northern Europe and North America and flourish in acidic, nutrient-poor soils. They are typically found in wooded areas and heathlands. These berries are valued for their strong flavor and deep color, making them a favorite addition to jams, jellies, and desserts [58].

Bilberries are well-known for their health advantages, owing to their high concentration of anthocyanins, a flavonoid that gives them their rich blue color. These chemicals have potent antioxidant effects, which assist in neutralizing free radicals and minimize oxidative stress in the body. Bilberries have long been used to improve vision and treat eye problems like night blindness and macular degeneration. Furthermore, their anti-inflammatory, antidiabetic, and cardiovascular benefits have been well-documented in modern research. Regular consumption may also support cognitive function and reduce the risk of age-related diseases.

Bilberries often known as European blueberries, contain a variety of bioactive chemicals, including UA. The concentration of UA in bilberries is predominantly found in their skins, however in fewer amounts than in apple peels. Depending on the growing circumstances and maturity, bilberries contain 10–30 mg of UA per 100 g of fruit. Bilberries are a

lesser-known but highly effective source of UA, a triterpenoid with numerous pharmaceutical applications. Their unique mix of UA and anthocyanins enhances their health benefits, which range from better vision and cardiovascular health to anti-cancer and neuroprotective properties. This establishes bilberries as a functional food with enormous promise in nutraceuticals and dietary supplements

3.6. Cranberries

Cranberries (Vaccinium macrocarpon) are tiny, tart, and brilliant red berries from the Ericaceae family. Native to North America, these evergreen bushes thrive in acidic bogs and marshes [59]. Cranberries are frequently consumed in numerous forms, including juice, dried fruit, sauces, and dietary supplements, especially during festive seasons such as Thanksgiving.

Cranberries are known for their high concentration of proanthocyanidins, a type of polyphenol that has powerful antioxidant and antibacterial activities. These chemicals are important in the prevention of urinary tract infections (UTIs) because they prevent bacteria, such as E. coli, from adhering to the urinary tract lining. Furthermore, cranberries have been linked to enhanced heart health, less inflammation, and digestive wellness. According to emerging studies, they may potentially have anticancer and neuroprotective characteristics, which would increase their medicinal potential. Cranberries (Vaccinium macrocarpon) are well-known for their high quantities of bioactive chemicals, including UA, which is found largely in the berries' skins. The content of UA in cranberries varies from 8 to 25 mg per 100 g of fresh fruit, depending on growth conditions and variety. Cranberries are a nutrient-dense source of UA, which compounds their already amazing health advantages. Cranberries are a diverse functional food due to the synergistic impact of UA and other bioactive substances, which benefit urinary tract health, cardiovascular health, and neuroprotection. This makes cranberries a good choice for nutraceuticals, dietary supplements, and medicinal uses.

3.7. Holy basil

Holy basil (*Ocimum sanctum* or *Ocimum tenuiflorum*), often known as tulsi, is a highly valued Ayurvedic plant from the Lamiaceae family. This aromatic plant is native to India and is commonly grown in tropical and subtropical countries for its medicinal, culinary, and spiritual properties. The plant normally develops to be 30–60 cm tall and has little purple or white blooms [60]. Holy basil is prized for its adaptogenic characteristics, which help the body deal with stress and restore balance. Its leaves contain several bioactive chemicals, including eugenol, rosmarinic acid, and apigenin, which aid in its anti-inflammatory, antioxidant, and antibacterial properties. Holy basil has traditionally been used to treat respiratory, digestive, and skin ailments. Modern research demonstrates its ability to lower cortisol levels, improve mental clarity, and promote immunity. Its hepatoprotective, anti-diabetic, and cardioprotective effects contribute to its standing as a holistic treatment [61].

Holy basil has numerous medicinal components, including UA. The plant's leaves and stems contain the majority of this triterpenoid. The concentration of UA in holy basil varies, but it usually ranges between 0.5 % and 1.5 % of the dry weight of the leaves, depending on cultivation circumstances and plant development. Holy basil contains a high concentration of UA, which contributes to its adaptogenic, antibacterial, and antioxidant effects. From stress relief to liver protection, cardiovascular health, and cancer prevention, the synergistic benefits of UA and other bioactive chemicals in holy basil make it an invaluable herb in both traditional and modern medicine. Its versatility makes it a strong choice for nutraceuticals, nutritional supplements, and medicinal applications [62].

3.8. Thyme

Thyme (*Thymus vulgaris*), a perennial herb from the Lamiaceae family, is endemic to the Mediterranean. Thyme, with its woody branches, tiny leaves, and exquisite purple blossoms, is a popular culinary herb that imparts a warm, earthy flavor to a wide range of meals. It is also an important element in herbal drinks, essential oils, and traditional treatments [63]. Thyme's health advantages come from its high concentration of thymol, an essential oil with strong antibacterial and antiseptic qualities. The herb has been used for millennia to treat respiratory problems like coughs, bronchitis, and sore throats. Thyme also has antioxidant, anti-inflammatory, and antifungal properties, making it beneficial for immune function and skin health. Recent research reveals that thyme may aid with digestion, lower blood pressure, and boost cognitive function, underscoring its therapeutic versatility.

Thyme a popular culinary and medicinal herb, has UA as one of its main bioactive components [64]. UA is mostly found in thyme leaves and flowers, with concentrations ranging from 0.3 % to 1.0 % of dry weight, depending on plant species, growth conditions, and harvest time. Thyme is high in UA, which enhances its medicinal and culinary properties. From respiratory and cardiovascular health to antibacterial activity, skincare, and neuroprotection, thyme's synergistic benefits of UA and other components make it an adaptable herb for traditional medicine, modern therapies, and functional foods. Its wide range of applications positions it as a valuable ingredient in nutraceuticals, dietary supplements, and wellness products [65].

3.9. Oregano

Oregano (*Origanum vulgare*), another member of the Lamiaceae family, is a perennial herb native to the Mediterranean. Oregano, known for its strong flavor and perfume, is a common ingredient in Mediterranean cuisine, particularly in sauces, marinades, and meat preparations. The dried leaves are especially popular as a spice in Italian, Greek, and Mexican dishes [66]. Oregano has numerous bioactive components, including carvacrol and thymol, which contribute to its antibacterial, antifungal, and antioxidant activities. These chemicals have been found to prevent the growth of bacteria such as Salmonella and E. coli, as well as fungi like Candida albicans. Oregano oil is frequently used in alternative medicine due to its immune-boosting properties and as a natural treatment for colds, flu, and respiratory infections. The plant also has anti-inflammatory and anticancer properties, which support its historic use to promote overall health and well-being.

Oregano, a popular culinary and medicinal herb, is a rich source of UA. This bioactive triterpenoid is found primarily in the leaves and flowers of oregano, with concentrations typically ranging from 0.4–1.2 % of the dry weight, depending on the variety, growth conditions, and harvest timing. Oregano, a high-quality source of UA, provides numerous health benefits, including antibacterial and anti-inflammatory actions, as well as cardiovascular and neurological qualities. Its applications range from culinary to nutraceuticals, dietary supplements, and medicinal formulations. With its varied properties, oregano remains an important herb in both traditional and modern medicine [67].

4. Pharmacological properties of UA

UA is a bioactive compound found in various healing plants, and was historically utilized in folk medicine long before its active therapeutic properties were fully understood [68]. Initially, UA was considered pharmacologically inactive, leading to its primary use as an emulsifier in medicinal, cosmetic, and food applications, often in the form of salts like potassium or sodium ursolates. However, emerging research has demonstrated that UA possesses a wide range of therapeutic benefits, both topically and internally. One of the key advantages of UA is its low toxicity profile. It is considered safe for dermatological use, with

minimal risk of acute or chronic toxicity, and is not classified as a primary irritant or sensitizer. Due to these favorable safety characteristics, it has gained popularity in cosmetic formulations. UA, along with its isomer oleanolic acid, has been recommended as a treatment for skin cancer in Japan, and topical formulations containing UA have been patented in the country for skin cancer prevention [69].

Beyond its dermatological benefits, UA exhibits a broad spectrum of pharmacological activities (Table 2). It is known for its hepatoprotective effects, helping to protect the liver from damage and support its detoxification functions. Additionally, UA has demonstrated significant antitumor properties, showing promise in the treatment of various cancers. Other therapeutic benefits include its anti-hyperlipidemic effects (reducing blood lipid levels), antioxidant properties (protecting cells from oxidative damage), and antiulcer activities (promoting gastric protection). Furthermore, UA has been shown to possess antimicrobial, anti-herpes, anti-atherosclerotic, hypotensive, anti-hyperglycemic, antinociceptive, and anti-HIV properties, highlighting its versatility as a medicinal compound. As interest in UA grows, there is a pressing need for sustainable methodologies to meet the increasing demand for this valuable compound. Traditional extraction methods, while effective, can be resource-intensive and environmentally taxing. Thus, more sustainable production approaches, including biotechnological methods like microbial fermentation and enzymatic synthesis, are being explored to reduce costs and environmental impact while maintaining high-quality yields of UA for pharmaceutical, cosmetic, and food applications [70].

4.1. Anti-cancer effects of UA

UA is a triterpenoid found in plants like rosemary and apples and shows strong anti-cancer potential through several mechanisms. It induces cell cycle arrest and apoptosis, inhibiting cancer cell growth and survival. UA is also modulating key signaling pathways, including NF-kB and MAPK, which are involved in inflammation, metastasis, and cell proliferation [82]. It reduces cancer cell migration and invasion by downregulating matrix metalloproteinases (MMPs) and suppresses angiogenesis, starving tumors by inhibiting blood vessel formation. Additionally, it enhances the effectiveness of chemotherapy, making it a promising candidate for cancer treatment, both as a stand-alone therapy and in combination with conventional drugs.

Table 2
Pharmacological effects and their proposed mechanisms.

S. No	Pharmacological effects	Proposed mechanism
1	Hepatoprotection	i. Protection against chemically induced liver necrosis [71]. i. Reduction of lipid peroxidation i. Modulation of the handling of acetaldehyde [72]. i. Induction of endogenous antioxidants [73].
2	Anti-inflammation	i. Increased vascular permeability i. Limitation of histamine release [74]. i. Lowered lipoxygenase and cyclooxygenase activity [75]. i. Inhibition of elastase [76].
3	Anti tumor Activity	i. Inhibition of mutagenicity by benzo (a) pyrene or aflatoxin B1 [77]. i. Inhibition of covalent binding of benzo (a) pyrene to DNA [78]. i. Inhibition of 12-O-tetradecanoylphorbol−13-acetate-induced Epstein-Barr virus activation [77]. i. Suppression of skin tumor promotion by TPA. v. Inhibition of tyrosine kinase [78]. v. Enhancement of the tumor necrosis factor-α [79].
4	Anti-hyperlipidemia	i. Prevention of experimental atherosclerosis [80]. i. Reduction of blood cholesterol and low-density lipoproteins [81]. i. Increase in blood high-density lipoproteins.

4.2. Anti-obesity/anti-diabetic effects of UA

UA is found in various plants and shows promising anti-obesity and anti-diabetic effects [83]. It reduces fat accumulation by inhibiting the differentiation of preadipocytes and enhances fat breakdown by activating lipolytic enzymes. UA is also boosting metabolic rate and thermogenesis, contributing to weight loss [84]. In diabetes management, it improves insulin sensitivity, lowers blood glucose levels, reduces insulin resistance, and positively modulates lipid profiles. Additionally, it protects pancreatic beta cells from damage, supporting effective insulin production. These multi-faceted actions highlight its potential as a therapeutic agent for obesity and diabetes [85].

4.3. Effects of UA on cardiovascular disease

UA is found in medicinal plants and offers significant cardiovascular benefits [86]. It lowers total cholesterol, LDL cholesterol, and triglycerides while increasing HDL cholesterol, thus reducing cardiovascular disease risk. UA inhibits atherosclerosis by reducing LDL oxidation and inflammation, enhances endothelial function, and protects against endothelial injury [87]. It also possesses anti-hypertensive effects by promoting vasodilation and modulating the renin-angiotensin system. Additionally, its antioxidant properties reduce oxidative stress and protect cardiac tissue from ischemic injury [88]. These multi-faceted effects highlight UA's potential in cardiovascular health management and prevention.

4.4. Effects of UA on brain

UA has demonstrated significant neuroprotective benefits, making it a promising candidate for supporting brain health and combating neurodegenerative diseases. Acting as a potent antioxidant, it helps reduce oxidative stress and neuroinflammation, which are key factors in cognitive decline and neurological disorders. UA also enhances cognitive functions such as learning and memory by promoting neurogenesis and synaptic plasticity. Additionally, it shows the potential to protect against Alzheimer's disease by preventing the buildup of toxic proteins in the brain. Beyond cognitive benefits, UA alleviates anxiety and stress by modulating the HPA axis, and it protects neurons from excite toxicity and mitochondrial dysfunction, both of which contribute to neuronal damage. These multifaceted neuroprotective actions underscore the therapeutic potential of UA for brain health and neurodegenerative diseases [89–92].

4.5. Effects of UA on exercise capacity

Recent studies have shown that UA may enhance exercise capacity by activating molecular pathways such as sirtuin-1 and PGC-1α, which are involved in energy metabolism and mitochondrial function. This activation is thought to lead to increased physical performance, improved cardiovascular health, and a better-resting heart rate. However, conflicting results have emerged, with some studies finding no significant improvements in exercise capacity. For example, research by [93–95] showed no enhancements in skeletal muscle strength or key signaling pathways related to exercise in subjects supplemented with UA. These discrepancies suggest that while UA may offer potential benefits for exercise performance, further investigation is needed to conclusively determine its effectiveness and clarify the conditions under which it may be most beneficial [96].

5. Conclusion

A naturally occurring triterpenoid molecule, UA has a variety of pharmacological characteristics and possible medical uses. Because of

its anti-inflammatory, antioxidant, and antibacterial properties, UA, which is present in a variety of plant species such as apple peel, rosemary, and betel leaves, has long been utilized in traditional medicine. These assertions have been supported by recent studies, which show that UA may help treat chronic illnesses like cancer, neurological disorders, metabolic problems, and liver diseases. Furthermore, UA has demonstrated the potential to boost cardiovascular health, maintain cognitive health, and increase exercise capacity. To completely understand its mechanisms of action, improve its delivery, and validate its effectiveness in human clinical trials, more study is necessary. UA is still a potential natural substance with a variety of therapeutic uses that call for more research and development.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Thirugnanasambandham reports was provided by TNAU. Thirugnanasambandham reports a relationship with Tamil Nadu Agricultural University that includes:. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was funded by Vinayaka Missions Research Foundation (VMRF) Seed Money Research grant. The Grant number is VMRF/Research/SeedMoney/2022-23/VMKVASC-1.

Data availability

The data that has been used is confidential.

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