

PHARMACOLOGICAL SIGNIFICANCE AND TOXICITY OVERVIEW OF OLEANOLIC ACID ISOLATED FROM *LANTANA CAMARA* ROOTS

NAVIKA GUPTA^{1*}, SUMER SINGH², ANU T. SINGH³, MANU JAGGI³

¹Department of Zoology Singhania University Pachari Kalan, Bari, Rajasthan, India. ²Department of School of Basic and Applied Sciences, Singhania University, Jhunjhunu, Rajasthan, India. ³Department of Management, Dabur Research Foundation, Ghaziabad, Uttar Pradesh, India.

*Corresponding author: Sumer Singh; Email: sumer@singhaniauniversity.ac.in

Received: 11 November 2025, Revised and Accepted: 18 January 2026

ABSTRACT

Preclinical Evidence on Oleanolic Acid from *Lantana camara*

Several therapeutic plants contain oleanolic acid (OA), a pentacyclic triterpenoid. Its drugs protect the liver, reduce inflammation, prevent diabetes, and fight cancer. *Lantana camara* roots are rich in OA, making them a promising medicine source. From 2000 to Up to present mid-2024, this study includes all published research on *L. camara* root OA, including phytochemical composition, pharmacological activity, toxicological evaluations, and mutagenicity assessments. We aggregated PubMed, Scopus, ScienceDirect, and Google Scholar data to find therapeutic relevance and safety margins. We thoroughly searched databases using relevant keywords. OA modulates oxidative stress pathways and detoxifying enzymes to protect the liver, and sub-chronic and acute toxicity studies in Wistar rats showed no mortality or adverse histopathological changes up to 2000 mg/kg. Ames tests showed its non-mutagenicity. However, insufficient clinical and chronic exposure investigations, poor water solubility, and bioavailability hinder translational applicability. The review finds that *L. camara* OA has promising lead phytotherapeutic potential, but more *in vivo* investigations and formulation improvements are needed to prove its efficacy and safety.

Keywords: Oleanolic acid, *Lantana camara*, Pentacyclic triterpenoid, Pharmacology, Toxicity, Mutagenicity.

© 2026 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2026v19i2.57375>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>

INTRODUCTION

Plant-based compounds have inspired or originated roughly 60% of clinically utilized medicines. Triterpenoids (triterpenes) [1-3], a structurally diverse family of secondary metabolites, have several therapeutic effects [4]. Their anti-inflammatory [5], anticancer, antiviral, hepatoprotective [6] antitumor-promotion effect [7], and antidiabetic [8] properties have been extensively studied [9-11]. This stresses the importance of cautious and informed medical use and their significant therapeutic potential.

Oleanolic acid (OA), a pentacyclic triterpenoid, has several therapeutic uses and is found in various plants. Fruit and leaf waxes include it to protect plants from dangerous microorganisms and other environmental pressures [12]. Over the past 30 years, OA has gained popularity because to its wide plant source availability, low toxicity, and broad therapeutic range [13-15].

A widely widespread tropical and subtropical plant, *Lantana camara* L. [16] (family: Verbenaceae) (Fig. 1), has been intensively investigated and remains a pharmacologically promising source. Ethnomedicine has utilized *L. camara* parts to treat wounds (wound healing) [17,18], fever, asthma, and gastrointestinal issues [19]. The roots of *L. camara* are rich in pentacyclic triterpenoids (Fig. 2), including OA, a significant bioactive [20-23] ingredient discovered by chromatographic and spectroscopic techniques [24,25]. Even though *L. camara* has many traditional medical uses; its leaves can be poisonous [26-29] to grazing animals and cause hepatotoxicity [30,31]. Due to its dual nature, long-term toxicity studies, bioavailability assessments, and safety evaluations [32] are needed to distinguish the toxicity of the crude plant from that of its isolated constituents, particularly OA [33,34].

When determining if bioactive substances [35] are safe to use, toxicological studies are crucial. Research on the oral toxicity of both single and multiple doses in rats is necessary to develop [36]. No-Observed-Adverse-Effect Levels (NOAELs) and Maximum Tolerated Doses (MTDs), as per OECD recommendations [37]. Investigations into the long-term exposure of OA extracted [38] from *L. camara* roots have revealed that acute and sub-chronic toxicity studies in Wistar rats resulted in no mortality at doses up to 2000 mg/kg in a single administration, suggesting a wide safety margin[39,40]. Furthermore, sub-chronic exploratory studies showed safety at doses of 1000 mg/kg body weight, with hematological and biochemical parameters remaining within normal ranges. Histopathological examinations of vital organs, such as the liver, kidneys, and spleen revealed no treatment-related abnormalities or adverse changes.

In addition to systemic toxicity, the mutagenic potential of new therapeutic candidates must also be thoroughly assessed. Genotoxic and mutagenic compounds pose a potential risk of mutagenic compound, or heritable genetic damage [41]. For assessing mutagenicity, the Ames test, which uses TA98 and TA100, two strains of *Salmonella typhimurium* that are histidine-dependent, is still considered the gold standard [42]. S9 metabolic activity or not, the Ames test on *L. camara* root OA did not show a statistically significant increase in revertant colonies. Thus, OA is non-mutagenic under test circumstances [43]. These findings support research showing that triterpenoids, including OA, are seldom genotoxic or mutagenic.

OA has been extensively researched in chemically induced liver damage [45] models for its hepatoprotective effects [44]. Its therapeutic effectiveness comes from modulating oxidative stress, detoxifying enzymes, and pro-inflammatory signaling pathways. Recently, OA has been shown to induce apoptosis, prevent metastasis, and decrease angiogenesis in numerous cancer cell lines [46]. OA has been approved



Fig. 1: *Lantana camara* plant



Fig. 2: Roots of *Lantana camara*

in China as an over-the-counter oral liver problem therapy for over two decades, proving its therapeutic relevance and safety.

OA drug development confronts several obstacles despite its medicinal potential [47-50]. No long-term exposure, pharmacokinetic data, limited water solubility, or oral bioavailability hinder clinical translation. Overcoming these limits requires pharmacological, biochemical, toxicological, formulation [51], and bioavailability investigations.

The efficient extraction of OA from *L. camara* roots makes this neglected botanical source useful. Systematic toxicological and pharmacological studies of OA can elucidate *L. camara*'s toxicity and its phytoconstituents' safety. This study wants all phytochemical [52], pharmacological [53], and toxicological data [54,55] on *L. camara* foliage-extracted OA. This paper evaluates scientific facts, stresses OA's therapeutic potential, safety profile, information gaps, and future research to establish it as a safe and effective lead chemical for drug discovery and development.

METHODS

The literature was evaluated using Google Scholar, Scopus, and PubMed. The search terms were "oleanolic acid," "*Lantana camara*," "pentacyclic triterpenoid," "toxicity," and "pharmacology." The study examined the medicinal, pharmacological, and toxicological effects of OA, primarily from *L. camara* roots.

The phytochemical composition, biological activity [56], and safety of OA, along with the Comparative Toxicological Profile: *L. camara* (whole plant) vs. OA were summarized from peer-reviewed studies and reports. Comparative evaluation of OA: Potency, Pharmacological Efficacy, and Inter-Study Variability Across Experimental Models were done summarized from peer-reviewed studies and reports. We discussed study gaps, future directions, and *L. camara*'s ecological value as a natural OA source based on the data.

Traditional uses

L. camara is traditionally used as a decorative plant, while it is also known as an invasive [57] plant in many tropical and invasive in many tropical/subtropical regions [58-60] it forms dense thickets that displace native flora and alters ecosystem. A wholesome work is done in India on the extract of plants and roots, leaves are used as an antimicrobial [61-64], nematocidal. Oil is used as a wound healing activity. The plant is used to cure a lot of respiratory order. The fruits are used in rheumatism, fistula, tumours, and pustules. The roots are used in rheumatism, malarial [65-70]

Phytochemistry of OA

A pentacyclic triterpenoid (3 β -hydroxyolean-12-en-28-oic acid) called oleanolic acid (OA) (Fig. 3) is a member of the oleanane class of secondary metabolites [71]. It possesses a hydroxyl group at C-3 and a carboxylic group at C-28, which contribute to its amphiphilic and bioactive nature [72,73]. OA is widely distributed in plants, such as olive (*Olea europaea*), ginseng (*Panax ginseng*), apples, plums, and the roots [41,42] of *L. camara*, which serve as a major source for extraction. Traditional medicine considers OA hepatoprotective and anti-inflammatory. Ethanol or methanol extraction and chromatographic purification are normal for *L. camara* roots [74,75]. Advanced methods include ultrasound-assisted and supercritical carbon dioxide extraction yield more and are more environmentally friendly. Fourier transform infrared (FTIR), mass spectrometry (MS), and nuclear magnetic resonance (NMR) verify structural purity, whereas high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS) quantify it. OA biosynthesis involves the mevalonate (MVA) route, including acetyl-CoA, squalene, and β -amyrin intermediates catalyzed by cytochrome P450 oxidases. Reported yields of 0.5–1.2% in *L. camara* roots suggest its potential as a renewable pharmaceutical and phytochemical source [76].

Natural occurrence

OA occurs extensively in higher plants, including fruits, vegetables, and medicinal herbs. High amounts are present in olive leaves (*O. europaea*), ginseng (*P. ginseng*), apples, and plums [19]. In ethnomedicine, OA is usually linked to hepatoprotective and anti-inflammatory activities in Indian and traditional Chinese medicine systems [76-78]. The *L. camara* roots have been found to be a rich and renewable source of OA, and hence they can be considered viable raw material for industrial extraction [79].

Extraction methods

The extraction of OA from *L. camara* roots and other plants typically involves solvent extraction techniques. The process typically begins with an active extraction using methanol or ethanol and continues with partitioning using increasingly polar solvents commonly employed in chromatography, such as hexane and ethyl acetate or dichloromethane and methanol. After drying, the root is crushed into a powder. The triturated material is mixed with a solvent in a 1:5 or 1:10 ratio (Fig. 4), which undergoes a solid extraction process using a reflux apparatus for 4–6 h at a moderate temperature of 50–60°C. After extraction, the mixture is filtered to remove solid residues or dirt. Then, under reduced pressure, the solvent is evaporated using a rotary evaporator, leaving behind a crude extract. This raw extract is then purified using column chromatography, with silica gel as the stationary phase. A solvent gradient, with hexane and ethyl acetate or dichloromethane and methanol, is employed to differentially separate OA from the other substances. Subsequent evaporation produces a final formulation

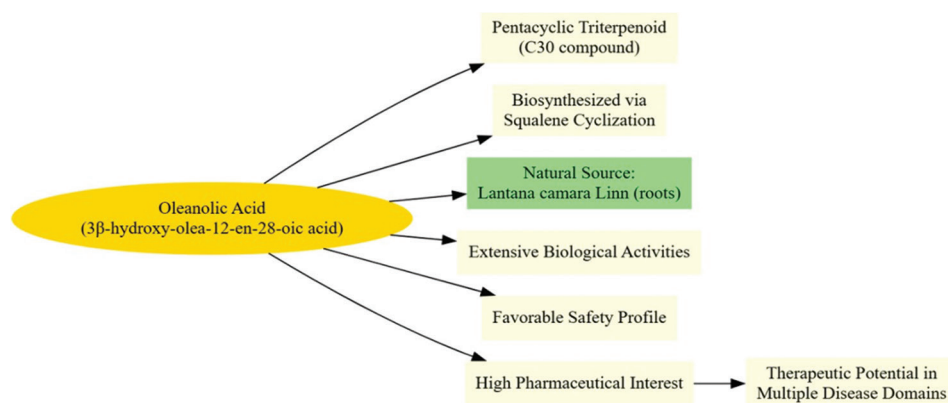


Fig. 3: Overview of oleanolic acid: Structure, origin and pharmaceutical significance

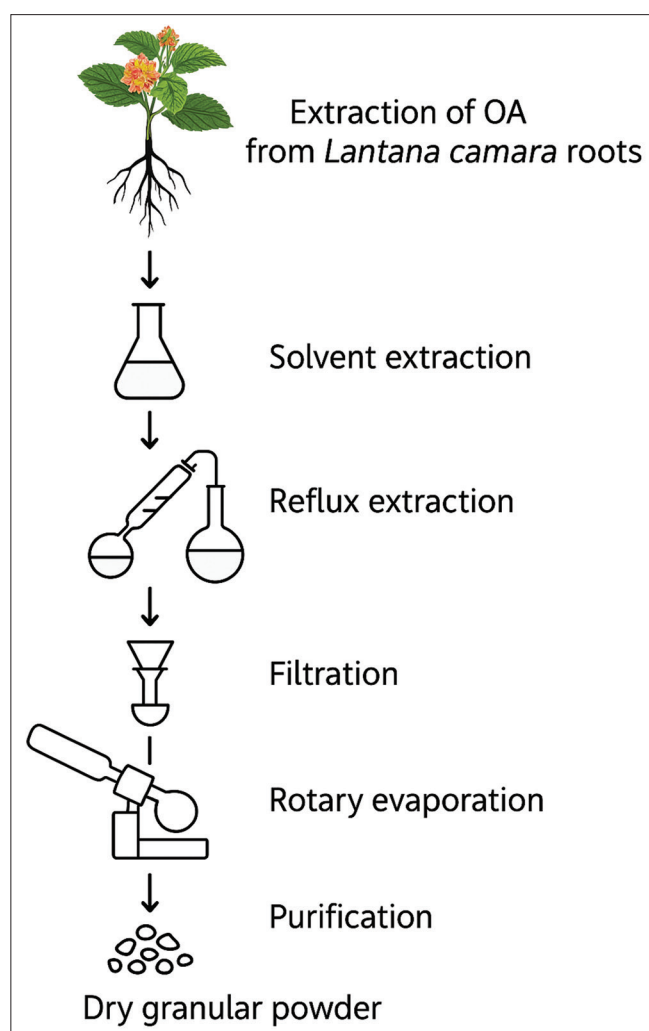


Fig. 4: Extraction process of oleanolic acid

of dry granular powder [80]. Better yields and less environmentally harmful chemistry are the results of these and other documented approaches, such as ultrasonic-assisted extraction and supercritical CO₂ extraction [81]. Recent research on *L. camara* roots identified ethanolic extraction with subsequent chromatographic fractionation to give a purified OA fraction, as identified by analytical characterization [82,83]. Efficiency of extraction varies with solvent polarity, part of the plant, and condition of drying.

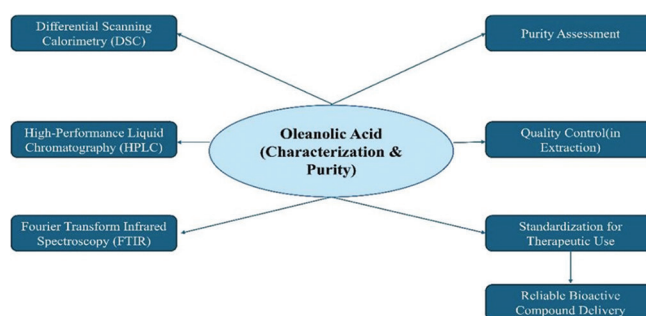


Fig. 5: Analytical characterization of oleanolic acid

Isolation and purification

Isolating OA is accomplished via column chromatography, which uses silica gel, or high-performance liquid chromatography, which uses HPLC. The use of crystallization methods allows for the last stage of purification.

Structural purity is critical since triterpenoids are usually found in association with ursolic acid, which shares similar pharmacological activity [84]. Today, cutting-edge analytical characterization techniques, including differential scanning calorimetry, HPLC [85,86] (Fig. 5), and FTIR spectroscopy allow for the precise identification and determination of OA's purity. These innovations improve extraction quality control and therapeutic preparation standardization, ensuring bioactive constituent delivery [87-95].

Analytical characterization

Several powerful analytical tools verify OA's authenticity and purity:

- Fourier transform infrared spectroscopy can identify functional groups, such as hydroxyl (-OH) and carboxyl (-COOH) vibrations
- MS determines molecular weight ($m/z = 456$ for OA)
- NMR (¹H-NMR, ¹³C-NMR) reveals OA structure. Quantitative plant extract analysis uses HPLC and GC-MS.

Biosynthetic pathway

Plants produce OA from MVA (Fig. 6). The process begins with acetyl-CoA and continues to squalene and β-amyrin. Oxidative alteration of β-amyrin leads to OA. These procedures need cytochrome P450 oxidases. The routes allow metabolic engineering in microbial OA production. OA levels vary by species and plant component, such as olive leaves (0.2–0.6% dry weight) and apple peels (0.4%). The yield of *L. camara* roots varies from ~0.5% to 1.7% dry weight, depending on extraction conditions [96,97].

Genetic and biotechnological developments

Recent molecular biology research has characterized key genes for β-amyrin synthase and some CYP450 enzymes responsible for OA

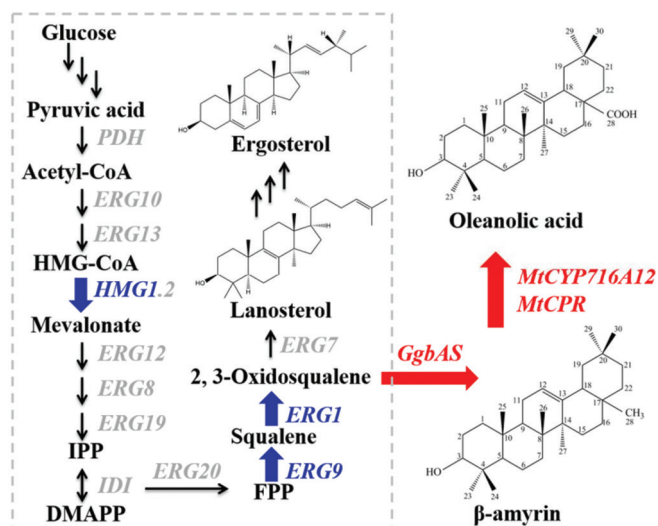


Fig. 6: Mevalonate pathway

biosynthesis. Gene engineering of these genes into microbial systems, such as *Saccharomyces cerevisiae* and *Yarrowia lipolytica*, has made it possible to produce OA within these organisms [98,99]. These findings demonstrate the potential of synthetic biology in the large-scale production of OA without recourse to plant extraction.

Ecological and plant defense functions

OA is a phytoalexin that assists plants in defending themselves against infection by pathogens [100,101], insects, and other forms of environmental stress. Its amphiphilic configuration destabilizes microbial membranes, leading to antifungal [102-105] and antibacterial resistance. This ecological function explains its ubiquity within different plant families.

Pharmacological and therapeutic potential of OA

The antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, antibacterial, and anticancer [106,107] effects of OA are the main reasons for its broad pharmacological range. Its potency and efficacy vary with species, cell type, dose, and administration route. *In vitro* studies [108] often show stronger effects than *in vivo*, and differences in extraction, purity, and protocols contribute to inter-study variability. Overall, OA demonstrates consistent beneficial effects, but their magnitude is study-dependent, highlighting the need for standardized models and dosing.

The chemical modulates nuclear factor-kappa B (NF-κB), nuclear factor erythroid 2-related factor 2 (Nrf2), and mitogen-activated protein kinase pathways, suppressing pro-inflammatory cytokines and enhancing cellular defense against oxidative stress. OA improves antioxidant enzyme [109] activity and lowers lipid peroxidation in chemically induced liver damage models, protecting the liver. In tumor cell lines, it activates caspase-3, inhibits metastasis, and stops angiogenesis. OA reduces blood glucose and enhances insulin sensitivity by modulating peroxisome proliferator-activated receptor gamma and metabolic enzymes, demonstrating antidiabetic effects. OA protects the heart and kidneys from oxidative and chemical damage. Multi-target activity and low toxicity make the molecule a promising phytopharmaceutical, but poor solubility and bioavailability hinder clinical translation. OA has significantly advanced over the past half a decade. Synthetic OA derivatives, such as bardoxolone methyl (CDDO-Me/RTA-402) also succeeded in reaching through large clinical programs of Phase-III trials, indicating a marked progress in translational interest, indicating safety/tolerability lessons from earlier studies (link to the survey: <https://clinicaltrials.gov/study/NCT03918447>); however, failed to proceed due to adverse cardiovascular outcomes. More recently done medicinal chemistry and SAR studies have produced numerous

OA derivatives and analogs with improved potency and drug-like properties. Several up-to-date scholarly articles have summarized these structure activity developments [110,111]. A significant thrust has been formulation science, lipid-based nanoparticles, nanosuspensions, peptide-assisted carriers and other nanoformulations have been developed to overcome OA's poor solubility and low oral bioavailability [112,113], with pre-clinical studies and formulation reviews reporting improved pharmacokinetics and enhanced *in vivo* efficacy. Early human pharmacokinetic and bioavailability data are now appearing (for example, the BIO-OLTRAD human study). OA is already described in the Chinese pharmacopeia/regulatory context as a liver-protective agent, illustrating both clinical testing and regional therapeutic use [114,115].

OA consistently shows strong pharmacological activity across anti-inflammatory, antioxidant, and other experimental models, though reported potency varies due to differences in extraction, purity, and study design. Despite this inter-study variability, its overall efficacy remains well supported, highlighting the need for more standardized protocols (Table 1).

Toxicological evaluation of OA

Acute toxicity

The toxicological safety of OA for therapeutic application is crucial. Oral toxic studies upon oral administration to rat models have confirmed that no mortality or behavioral issues appear, indicating a significant safety margin. Further validation came upon hematological [122] biochemical and organ-weight evaluations, which did not display any signs of changes even after 90 days of the OA administration in half dosages. Histopathology demonstrated standard vital organ architecture, ruling out systemic toxicity in the heart, liver, kidneys, and spleen.

An evaluation has also been made from the literature about *S. Typhimurium* strains TA98 and TA100 with and without S9 metabolic activation. Revertant colonies did not increase at any dose in this experiment, indicating OA is not mutagenic. These results are consistent with previous findings on pentacyclic triterpenoids, which generally exhibit low genotoxic potential. Overall, available evidence demonstrates that OA might possess a favorable toxicological and genetic-safety profile at an acceptable level, supporting its development as a safe phytochemical for long-term pharmacological and nutraceutical applications.

However, a broader reading of recent (2022–2025) literature reveals both supporting and contradictory toxicology signals that must be acknowledged. Multiple genotoxicity and mutagenicity-based studies report no clear mutagenic potential for OA in standard bacterial assays (TA98/TA100 ± S9) and conclude low genotoxic risk for isolated OA preparations [123].

Several well-conducted pre-clinical reports and reviews find minimal acute/sub-chronic toxicity at typical pharmacological doses and even at relatively high single doses in rodents, supporting a wide therapeutic index in short-term studies [124]. At the same time, multiple studies also document dose- and duration-dependent hepatotoxicity/cholestasis in rodents after repeated high-dose OA exposure, with FXR/BSEP-related bile-acid handling implicated as a mechanistic mediator, i.e., low doses are often hepatoprotective while long-term or very high dosing can impair bile acid transport and produce cholestatic injury [125]. Species, formulation, and route greatly modify outcomes. Targeted delivery and inhalation studies report favorable acute safety profiles for lung delivery in rats, while dietary or chronic oral exposures show more variable results across species (rodent vs. livestock/poultry models [126,127]). Nanoparticle or derivatization strategies that increase OA systemic exposure improve pharmacodynamics, but can also alter the toxicology profile, so formulation-driven pharmacokinetic changes must be accompanied by repeat-dose and chronic toxicology (including liver/biliary endpoints)

Table 1: Comparative evaluation of oleanolic acid: Potency, pharmacological efficacy, and inter-study variability across experimental models [116-121]

S. No.	Effect area	Model	Dose/Potency	Main outcome	Consistency across studies	References
1.	Hepatotoxicity (high dose only)	Mice	300–500 mg/kg	Cholestatic injury, ↑ bile acids	Seen only at very high doses	Lu et al. (2013)
2.	Hepatoprotective effect	CCl ₄ , APAP, α-amanitin models	25–100 mg/kg	Strong liver protection	Highly consistent across toxins	Feng et al. (2020)
3.	Anti-inflammatory effect	LPS-stimulated macrophages	1–20 μM	↓ TNF-α, IL-6, NO	Moderate variability by cell type	Iqbal et al. (2023)
4.	Anti-diabetic activity	STZ-diabetic rats	20–50 mg/kg	↓ Glucose, ↑ insulin sensitivity	Mild to moderate variability	Fan et al. (2015)
5.	Anti-oxidant/metal toxicity protection	HgCl ₂ injury model	25–100 mg/kg	↓ Oxidative stress	Limited but consistent evidence	Martín et al. (2007)
6.	Cholestasis protection	Bile-duct ligated rats	100 mg/kg	↓ Bile acids, ↓ inflammation	Strong consistency	Alqahtani et al. (2013)
7.	Anti-cancer activity	Cancer cell lines	5–50 μM	Anti-proliferative, apoptosis	High variability across cell types	Ouyang et al. (2022)

Keys: ↑: Increase, ↓: Decrease. CCl₄: Carbon tetrachloride, TNF-α: Tumor necrosis factor-alpha, IL-6: Interleukin-6, NO: Nitric oxide, STZ: Streptozotocin, APAP: Acetaminophen/Paracetamol, LPS: Lipopolysaccharide

rather than PD-only cases [128,129]. Translational caution is supported by clinical-stage lessons from related oleanane triterpenoid programs (e.g., bardoxolone methyl), where large trials revealed unexpected cardiovascular safety signals emphasizing the need for rigorous human pharmacokinetics, thorough dose-finding, and targeted organ safety monitoring in any OA development program [130].

Sub-acute/sub-chronic toxicity

Repeated-dose studies with OA and related pentacyclic triterpenoids generally show low toxicity at therapeutic doses. Some studies report mild, reversible changes only at high doses. Ninety-day studies on related triterpenes (e.g., UA) suggest acceptable safety but emphasize the need for long-term studies specifically on OA. No treatment-related side effects were seen at limited dosages up to a certain level in the *L. camara* OA research. This supports a favorable NOAEL region for short-term use. However, long-term studies (chronic, reproductive, and developmental) remain limited. While some limited data are available on the study of *L. camara* on Rat fertility [131].

L. camara is known to be toxic due to lantadenes that cause hepatotoxicity and photosensitization, leading to illness and mortality in animals. In contrast, isolated OA shows a much safer profile, with studies reporting low acute toxicity, hepatoprotective effects, and no mutagenicity. Thus, the plant's toxicity is linked to lantadenes, while OA itself is considered non-toxic under typical pre-clinical conditions (Table 2).

Mutagenicity and genotoxicity

Ames test and bacterial reverse mutation assay

Analyzing bacterial ames testing and reverse mutation, one of the most used methods for determining mutagenicity is the Ames test, which is also known as the bacterial reverse mutation assay. *S. Typhimurium* strains TA98, TA100, TA102, TA1535, and TA1537, as well as metabolic activation (S9), are utilized as needed. No mutagenic effects were seen in any of the strains tested for by OA. It failed to elicit point mutations regardless of the dosage studied and regardless of the presence or absence of metabolic activity. Therefore, it was determined that OA was non-mutagenic up to 5000 μg/plate based on the circumstances of this investigation.

Evidence for OA

Multiple studies indicate OA and many oleanane triterpenoids exhibit low or no mutagenic potential in the Ames assay and related genotoxicity screens. Specifically, OA isolated from *L. camara* roots was non-mutagenic across standard *Salmonella* strains (including tests

with S9 activation) in the author's characterization/mutagenicity study

Interpretation and limitations

While negative Ames results reduce concern for direct bacterial mutagenicity, they do not exclude other genotoxic mechanisms (chromosomal aberrations, *in vivo* genotoxicity); therefore, a battery of genotoxicity tests (*in vitro* mammalian cell genotoxicity and *in vivo* tests) is recommended for regulatory completeness facilitate better interpretation of results and establish appropriate safety margins. Evidence from pharmacology and toxicology suggests that OA is a promising therapeutic candidate with broad bioactivity and a favorable short-term safety profile. The OA isolated from *L. camara* roots, characterized chemically and shown to be non-mutagenic in Ames' testing, strengthens confidence for further development. Nevertheless, essential data gaps persist: (1) Chronic toxicity and carcinogenicity studies; (2) Reproductive and developmental toxicity; (3) Robust ADME/PK and human safety data; and (4) Improved formulations to overcome OA's bioavailability limitations. Clinical translation under GLP necessitates resolving these gaps, notably long-term safety and human research. Pharmacology and toxicology show OA has extensive bioactivity and short-term safety. *L. camara* root OA was chemically identified and non-mutagenic in Ames experiments, improving study confidence. OA's bioavailability issues need novel formulations, chronic toxicity and carcinogenicity studies, reproductive and developmental toxicity, ADME/PK, and human safety data. GLP clinical translation must address long-term safety and human research limitations. We would also like to highlight that the purification studies of OA from *L. camara* are scarce in number, due to which the topic is not covered in depth within this review. Due to this limitation, no chronic (>6 months), reproductive, or carcinogenicity studies are covered in depth, and future studies should focus on this topic.

DISCUSSION AND FUTURE PROSPECTS

L. camara roots are a practical OA source because the plant is widespread, low-cost, and often removed as invasive biomass, and metabolomic analyses confirm OA among its abundant triterpenoids, making root valorization an attractive, sustainable feedstock for local extraction/lead-finding [141,142]. Without any doubt, olive-leaf/pomace and apple-peel supply chains are already industrialized, better standardized (and nutraceuticals exploited), and have clearer GRAS/nutritional pathways for near-term commercialization; however, all sources share the same translational constraints of low oral bioavailability and variable yields unless paired with improved formulation or derivatization [143]. OA is a potential treatment due to its efficacy and safety. Its anticancer [144], antioxidant, anti-inflammatory, antimicrobial, and hepatoprotective properties

Table 2: Comparative toxicological profile: *L. camara* vs. Oleanolic acid [132-140]

Parameter	<i>L. camara</i> (Whole plant/ crude extract)	Oleanolic acid (isolated compound)	Key references
Primary toxic constituents	Lantadene A, Lantadene B (pentacyclic triterpenoids known for hepatotoxicity)	No known hepatotoxic constituents; shows hepatoprotective properties	Seawright and Hrdlicka (1977)
Toxicological profile	Highly toxic; induces cholestatic hepatotoxicity, photosensitization, GI disturbances, and mortality in livestock and rodents	Low toxicity; high LD ₅₀ (>5 g/kg in rodents); protective against CCl ₄ - and paracetamol-induced liver injury	Chen <i>et al.</i> (2015)
Mechanism of toxicity/safety	Lantadenes inhibit bile flow, cause hepatocellular necrosis, and oxidative stress	OA enhances antioxidant defenses, stabilizes liver membranes, and reduces oxidative stress	Kaya <i>et al.</i> (2010); Santos <i>et al.</i> (2012)
Dose range associated with toxicity/safety	Toxicity observed at 50–200 mg/kg of lantadenes in animal models	OA shows no significant toxicity up to 2,000–5,000 mg/kg oral dosing	Ghisalberti (2000); Nyarko and Addy (1990)
Pharmacological relevance	Limited due to toxicity; crude plant preparations are unsafe	Broad pharmacological actions: Anti-inflammatory, hepatoprotective, antidiabetic, anticancer	Pollier and Goossens (2012); Huang <i>et al.</i> (2006)
Outcome in pre-clinical models	Liver damage, increased ALT/AST, jaundice, and mortality	Reduction in ALT/AST, improved histopathology, and strong protective effects	Liu <i>et al.</i> (1995); Zhang <i>et al.</i> , (2011)
Safety recommendation	Not recommended for therapeutic use due to unstable and toxic profile	Considered safe; widely explored as a lead compound in drug development	ESCOP Monographs; WHO phytochemical safety review

L. camara: *Lantana camara*, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, WHO: World Health Organization, CCl₄: Carbon tetrachloride, GI: Gastrointestinal, LD₅₀: Lethal dose 50%

result from NF- κ B and Nrf2 pathway modulation. Several recent studies and reviews temper enthusiasm and point to clear limitations that must be acknowledged. Quantitative pharmacokinetic work in rodents and recent reviews report very low oral bioavailability (for example, measured oral bioavailability as low as ~0.7% in rat studies), which helps explain inconsistent efficacy between models and motivates formulation research; thus, its clinical use is hindered. Human pharmacokinetic data are still sparse, and the controlled BIO-OLTRAD study (single-dose PK in healthy volunteers) illustrates detectable systemic exposure after an oral/food formulation but emphasizes that human exposure data remains limited and variable, so direct translation of many animal dosing regimens is uncertain. Several recent pre-clinical reports also document variable or absent effects at commonly used 'reasonable' doses in animal models or agricultural studies (for example, dietary OA showed limited impact on growth/performance end points in broiler studies and mixed results across other species), indicating that efficacy is not universal and depends strongly on dose, formulation, and model. Some studies flag safety and dose-related concerns (including cholestasis or liver index changes at high or long-term dosing in animals and the well-documented safety lessons from related synthetic oleanane triterpenoids), underscoring that "safe" in pre-clinical short-term studies does not guarantee safety in chronic human use [145]. Because of these contradictions, a major recent thrust in the literature has been on delivery and formulation strategies (nanoparticles, peptide carriers, lipid formulations, and other approaches) that demonstrably increase systemic exposure and tissue delivery in pre-clinical work, but these improved PK/PD profiles still require careful dose-finding and long-term toxicology before clinical claims can be solidified.

A focused comparison with structurally related pentacyclic triterpenoids (most commonly UA, but also betulinic and other lupane-type triterpenes) clarifies both shared opportunities and important differences [146]- OA and UA are constitutional isomers with highly similar pharmacology, both modulate NF- κ B, Nrf2, and other redox/inflammatory nodes, and show overlapping therapeutic activities in pre-clinical work. But recent comparative scholarly articles emphasize that outcome, potency, and translational readiness differ by molecule, preparation,

and indication [147,148]. Mechanistic and *in vivo* data indicate areas where UA currently has stronger or more consistent evidence. Several recent animal studies (and a 2023 gut-microbiome/metabolomics mouse study) identify UA as having reproducible anti-obesity and metabolic effects (reduced adiposity, improved insulin sensitivity, altered gut microbiota) that are less consistently reported for OA under comparable models and doses [149,150]. OA retains a comparative clinical advantage in hepatoprotection because of its long history of human use and productization in China and the emergence of human pharmacokinetics data, which provide at least preliminary human exposure and regulatory context that UA lacks at the same level. A major unifying limitation for both OA and UA is pharmacokinetics. Pharmacokinetics studies have shown low oral bioavailability for both triterpenoids in standard formulations (OA reported as low as ~0.7% in rodent work), which helps explain discordant preclinical results and argues that apparent inter-molecule differences sometimes reflect delivery/pharmacokinetics rather than intrinsic potency. Accordingly, 2022 to 2024 medicinal-chemistry and formulation studies have emphasized three parallel routes to translation: (1) Structural derivatization to improve potency and drug-like properties, (2) Nano/lipid/solubilizing delivery systems to raise systemic and tissue exposure, and (3) Head-to-head preclinical comparisons using standardized PK-matched dosing. Continuous efforts are still active with programs for both OA and UA derivatives and multiple nanoformulation approaches that improve exposure and PD readouts *in vivo*, but none yet provide definitive evidence that improved exposure uniformly translates to safe, reproducible clinical benefit. These comparative data between OA and UA suggests three practical recommendations for the field, (i) Where possible, perform head-to-head preclinical studies that match systemic exposure (dosing) when comparing to each other or other triterpenoids, (ii) Prioritize derivatization + formulation pipelines that report both pharmacokinetics and -dynamics endpoints (not anyone alone), and (iii) When moving to humans, choose indications and formulations guided by the molecule's strongest translational signal. It should also accompany early trials with intensive pharmacokinetics and liver/biliary safety monitoring. These steps will make comparative claims evidence-based instead of anecdotal and

will help determine whether scaffold choice (oleanane vs. ursane vs. lupane) materially changes clinical potential. Compiling all these facts, we can reach to the conclusion that future studies should therefore prioritize dose finding, validated human pharmacokinetic studies, standardized efficacy endpoints across models, and in-depth sub-chronic/chronic toxicology (including liver/biliary markers) alongside advanced formulation strategies to determine whether improved exposure translates into reproducible therapeutic benefit. Comparative analysis with comparable triterpenoids and well-structured clinical trials are also needed for safe OA usage, with the incorporation of new data to take a lesson from the failures. OA may be a safe, multi-targeted phytotherapeutic compound with better transport and pharmacology.

CONCLUSION

OA derived from *L. camara* roots presents a compelling profile as a lead phytotherapeutic compound, characterized by a range of promising pharmacological activities and a favorable short-term preclinical safety profile. Existing evidence, including acute and sub-chronic toxicity studies in rodent models and negative Ames test results, suggests a wide therapeutic index and low mutagenic potential under the conditions tested. However, significant data gaps that currently preclude a definitive declaration of its safety and efficacy for human use still remain unanswered. The promising preliminary findings are tempered by the absence of chronic toxicity, carcinogenicity, and clinical data. OA's well-documented challenges with poor aqueous solubility and low oral bioavailability represent a major translational hurdle that limits its therapeutic application. Therefore, the future trajectory for establishing OA as a viable therapeutic agent must prioritize rigorous, targeted research. Key priorities include conducting comprehensive chronic toxicity and carcinogenicity studies, advancing formulation strategies, such as nano-delivery systems to overcome bioavailability limitations, and validating its efficacy and safety in well-designed clinical trials. Only through such systematic efforts can the translational promise of OA be fully and reliably evaluated.

AUTHOR'S CONTRIBUTIONS

Navika Gupta: Conceptualization, writing, proofreading, funding acquisition, reviewing, and editing. Sumer Singh: Proofreading, reviewing, editing original draft, Anu T. Singh: Proofreading, reviewing, editing original draft, Manu Jaggi: Proofreading, reviewing, editing original draft.

ACKNOWLEDGMENT

We extend our sincere gratitude to all authors who have contributed equally.

CONFLICT OF INTERESTS

Authors declare that we have no conflict of interest.

FUNDING SOURCES

Not applicable.

REFERENCES

- Barton DH, De Mayo P. Triterpenoids. Part XV. The constitution of icterogenin, a physiologically active triterpenoid. *J Chem Soc.* 1954;887-900. doi: 10.1039/jr9540000887
- Barua AK, Chakrabarti P, Basu K, Basak A, Chakravarti S, Banerjee SK. Triterpenoids XLII. Further studies on the structure of lantanolic acid. *J Indian Chem Soc.* 1975;52:1112-3.
- Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. *J Nat Prod.* 2020;83(3):770-803. doi: 10.1021/acs.jnatprod.9b01285, PMID 32162523
- Saxena M, Saxena J, Khare S. A brief review on: Therapeutic values of *Lantana* plant. *Int J Pharm Life Sci (IJPLS).* 2012 Mar;3(3):1551-4.
- Iqbal M, Ali S, Bukhari N. Anti-inflammatory effects of *Lantana camara* leaf extracts in rheumatoid arthritis models. *J Inflamm Res.* 2023;16:245-53.
- Reddy S, Kumar A, Singh G. Hepatoprotective effects of *Lantana camara* in chronic liver diseases: A detailed study. *Liver Int.* 2023;43(4):1079-88.
- Shibata S. Chemistry and cancer preventing activities of ginseng saponins and some related triterpenoid compounds. *J Korean Med Sci.* 2001;16 Suppl: S28-37. doi: 10.3346/jkms.2001.16.S.S28, PMID 11748374
- Choudhury P, Singh S, Sharma N. Antidiabetic activity of *Lantana camara* in hyperglycemic animal models. *J Endocrinol Invest.* 2023;46(6):1121-30.
- Guo J, Huang M, Hou S, Yuan J, Chang X, Gao S, et al. Therapeutic potential of terpenoids in cancer treatment: Targeting mitochondrial pathways. *Cancer Rep (Hoboken).* 2024 Sep;7(9):e70006. doi: 10.1002/cnr2.70006, PMID 39234662, PMCID PMC11375335.
- Shanmugam MK, Dai X, Kumar AP, Tan BK, Sethi G, Bishayee A. Oleanolic acid and its synthetic derivatives for the prevention and therapy of cancer: Preclinical and clinical evidence. *Cancer Lett.* 2013;346(2):206-16. doi: 10.1016/j.canlet.2013.12.013
- Džubák P, Hajdúch M, Vydra D, Hustová A, Kvasnica M, Biedermann D, et al. Pharmacological activities of natural triterpenoids and their therapeutic implications. *Nat Prod Rep.* 2006;23(3):394-411. doi: 10.1039/b515312n, PMID 16741586
- Khan A, Khan S, Khan M. Oleanolic acid: A review on its pharmacological importance, pharmacokinetics, toxicity and analytical aspects. *J Drug Deliv Ther.* 2015;5(6):7-13. doi: 10.22270/jddt.v5i6.1161
- Pollier J, Goossens A. Oleanolic acid. *Phytochemistry.* 2012;77:10-5. doi: 10.1016/j.phytochem.2011.12.022, PMID 22377690
- Shanmugam MK, Dai X, Kumar AP, Tan BK, Sethi G, Bishayee A, et al. Oleanolic acid and its synthetic derivatives for the prevention and therapy of cancer: Preclinical and clinical evidence. *Cancer Lett.* 2014 May 1;346(2):206-16. doi: 10.1016/j.canlet.2014.01.016
- Guo Y, Han B, Luo K, Ren Z, Cai L, Sun L. NOX2-ROS-HIF-1 α signaling is critical for the inhibitory effect of oleanolic acid on rectal cancer cell proliferation. *Biomed Pharmacother.* 2017 Jan;85:733-9. doi: 10.1016/j.biopha.2016.11.091
- Wikipedia Contributors; 2024, December 22. *Lantana camara*. Wikipedia, the Free Encyclopedia. Available from: https://en.wikipedia.org/w/index.php?title=lantana_camara&oldid=1264560901
- Mekala S, Kumar Naresh M, Das L, Shetty N, Amuthan A, Vulli V, et al. Evaluation of wound-healing activity of ethanolic extract of *Lantana camara* in streptozotocin-induced diabetic rats. *Int J Pharm Pharm Sci (IJPPS).* 2014;6(1):631-3.
- Abdulla MA, Hassandarvish P, Ali HM, Noor SM, Mahmoud FH, Bashah NS, et al. Acceleration of wound healing potential by *Lantana camara* leaf extract in experimental rats. *Res J Med Sci.* 2009;3:75-9.
- Ghisalberti EL. *Lantana camara* L. (Verbenaceae). *Fitoterapia.* 2000;71(5):467-86. doi: 10.1016/S0367-326X(00)00202-1, PMID 11449493
- Kalita S, Kumar G, Karthik L, Rao KV. A review on medicinal properties of *Lantana camara* Linn. *Res J Pharm Tech.* 2012 June;5(6):711-5.
- Misra N, Sharma M, Raja K, Dangi A, Srivastava S, Bhattacharya SM. Chemical constituents and antifilarial activity of *Lantana camara* against human lymphatic filariid *Brugia malayi* and rodent filariid *Acanthocheilonema viteae* maintained in rodent hosts. *Parasitol Res.* 2006;100:439-48.
- Sastri BN. The Wealth of India, Raw Materials. Vol. 6. New Delhi: Council of Scientific and Industrial Research; 1962.
- Jannus F, Sainz J, Reyes-Zurita FJ. Principal bioactive properties of oleanolic acid, its derivatives, and analogues. *Molecules.* 2024;29(14):3291. doi: 10.3390/molecules29143291, PMID 39064870
- Begum S, Zehra SQ, Siddiqui BS, Fayyaz S, Ramzan M. Triterpenoids from the roots of *Lantana camara*. *Chem Pharm Bull.* 2014;62(2):148-52. doi: 10.1248/cpb.c13-00663
- Sousa EO, Almeida TS, Menezes IR, Rodrigues FF, Campus AR, Lima SG, et al. Chemical composition of essential oils of *Lantana camara* L. (Verbenaceae) and synergistic effect of the aminoglycosides gentamicin and amikacin. *Rec Nat Prod.* 2012;6:144-50.
- Black H, Carter RG. Lantana poisoning of cattle and sheep in New Zealand. *N Z Vet J.* 1985;33(8):136-7. doi: 10.1080/00480169.1985.35197, PMID 16031191
- Chopra RN, Badhwar RL, Ghosh S. Poisonous Plants of India. Vol. 11. New Delhi: Indian Council of Agricultural Research; 1965. p. 698-9.
- De Aluja AS. 'Mal de playa'-*Lantana camara* poisoning in cattle. *Vet Mex.* 1970;1(4):7-13.
- Da Silva FM, Couto ES. Experimental poisoning of cat tle by *Lantana*

- camara in the state of Pernambuco. Arquivos da es cola de Velerinaria. Universidade Federal de Minas Gerais. 1971;23:77-89.
30. Sharma OP, Makkar HP, Dawra RK. A review of the hepatotoxic plant *Lantana camara*. J Ethnopharmacol. 2007;96(1-2):135-52. doi: 10.1016/j.jep.2004.08.007
 31. Asija R, Kumar V, Sharma AK. Hepatoprotective activity of *Lantana camara* against carbon tetrachloride-induced hepatotoxicity in Wistar rat. Int J Pharm Erud. 2015;4:1-7.
 32. Barros LM, Duarte AE, Pansera Waczuk E, Roversi K, Da Cunha FA, Rolon M, et al. Safety assessment and antioxidant activity of *Lantana montevidensis* leaves: Contribution to its phytochemical and pharmacological activity. EXCLI J. 2017;16:566-82. doi: 10.17179/excli2017-163, PMID 28694758
 33. Venkatadri R, Guha G, Kumar R, Lazar M. Evaluation of cytotoxic potential of *Acorus calamus* rhizome. Res Ethnobot Leaf. 2009;13(6):839.
 34. Adama K, Adama B, Tamboura H, Amadou T, Laya S. *In vitro* anthelmintic effect of two medicinal plants (*Anogeissus leiocarpus* and *Daniellia oliveri*) on *Haemon Chuscontortus*, an Abosomal nematode of sheep in Burkina Faso. Afr J Biotechnol. 2009;4690:4695.
 35. Wu P, Song Z, Wang X, Li Y, Li Y, Cui J, et al. Bioactive triterpenoids from *Lantana camara* showing anti-inflammatory activities *in vitro* and *in vivo*. Bioorg Chem. 2020;101:104004. doi: 10.1016/j.bioorg.2020.104004, PMID 32629274
 36. Bahadure RS, Bijwal DL, Sadekar RD, Mode SG. Efficacy of Tefroli in prevention of experimental *Lantana* toxicity in calves. Indian J Vetmed. 1992;12:49-51.
 37. OECD. OECD Guidelines for the Testing of Chemical. Health Effects. Sec. 4. Paris: Organization for Economic Co-operation and Development; 2008. doi: 10.1787/9789264070843-en
 38. Kosior MW, Krzaczek JT, Matysik G, Skalska A. HPTLC-densitometric method of determination of oleanolic acid in the Lamiialbios. J Sep Sci. 2005;28:2139-43.
 39. Gupta N, Singh AT. Toxicological evaluation of oleanolic acid (pentacyclic triterpenoid) extracted from *Lantana camara* roots following oral exposure in Wistar rats. Asian J Pharm Clin Res. 2024 May;17(5):131-8. doi: 10.22159/ajpcr.2024.v17i5.49999
 40. Patel D. A comprehensive review:- Toxicological effect of common drug and poison on human physiology and analytical detection techniques to detect in biological samples- using instrumentation chromatography, biosensors and nanotechnology. Int J Adv Res. 2024;12:949-57. doi: 10.21474/IJAR01/19715
 41. ICH. Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use S2. Vol. R1. India: International Council for Harmonisation; 2011.
 42. Mortelmans K, Zeiger E. The Ames *Salmonella*/microsome mutagenicity assay. Mutat Res. 2000;455(1-2):29-60. doi: 10.1016/S0027-5107(00)00064-6, PMID 11113466
 43. Gupta N, Chandra S, Singh AT, Jaggi M. Characterization of *Lantana Camara* Roots (pentacyclic triterpenoid) and mutagenicity testing of extracted oleanolic acid using *Salmonella typhimurium*. Arch Clin Med Microbiol. 2022;1(1):20-30.
 44. Tsuchiya Y, Nakajima M, Yokoi T. Cytochrome P450-mediated metabolism of oleanolic acid and hepatoprotective effects. Drug Metab Dispos. 2012;40(7):1513-9. doi: 10.1124/dmd.112.044313
 45. Dhomse RS, Sanap TK, Gavhane PB, Vaidya SS. A review on *Lantana camara*: A valuable medicinal plant. Int J Creat Res Thoughts 2024;12:a711-21.
 46. Udayama M, Kinjo J, Nohara T. Triterpenoidal saponins from *Baptisia australis*. Phytochemistry. 1998;48(7):1233-5. doi: 10.1016/S0031-9422(98)00162-9, PMID 9680727
 47. Zhao G, Yan W, Cao D. Simultaneous determination of betulin and betulinic acid in white birch bark using RP-HPLC. J Pharm Biomed Anal. 2007;43(3):959-62. doi: 10.1016/j.jpba.2006.09.026, PMID 17084057
 48. Battase LD, Attarde DL. Phytochemical and medicinal study of *Lantana camara* linn. (Verbenaceae) - a review. Asian J Pharm Clin Res. 2021;14(9):20-7.
 49. Vrouwe JP, Burggraaf J, Kloppenburg M, Stuurman FE. Challenges and opportunities of pharmacological interventions for osteoarthritis: A review of current clinical trials and developments. Osteoarthritis Cartil Open. 2021;3(4):100212. doi: 10.1016/j.ocarto.2021.100212, PMID 36474768
 50. Ayeleso TB, Matumba MG, Mukwevho E. Oleanolic acid and its derivatives: Biological activities and therapeutic potential in chronic diseases. Molecules. 2017 Nov 13;22(11):1915. doi: 10.3390/molecules22111915.
 51. Tiwari P, Krishanu S. Preliminary physico - phytochemical & phyto cognostical evaluation of the leaves of *Lantana camara*. J Pharmacogn Phytochem. 2023;12(1):592-6.
 52. Ekpenyong CE, Akpan EE, Daniel AE. Phytochemical constituents, therapeutic applications and toxicological profile of *Cymbopogon citratus* Stapf (DC) leaf extract. J Pharmacogn Phytochem. 2014;3(1):133-141.
 53. Ghosh A, Mehta P. Yield variability of oleanolic acid in *Lantana camara*: A renewable pharmaceutical source. J Med Plants Stud. 2020;15(1):87.
 54. Sharma OP, Makkar HP, Dawra RK, Negi SS. A review of the toxicity of *Lantana camara* (Linn) in animals. Clin Toxicol. 1981;18(9):1077-94. doi: 10.3109/15563658108990337, PMID 7032835
 55. Singh V, Agrawal M, Nagda RK, Sharma MC, Mordia A. A case study of *Lantana camara* poisoning in Sirohi goat. Int J Rec Sci Res. 2018;9:27953-5.
 56. Gordon DR, Thomas DR. The spread of *Lantana camara* and its effects on biodiversity in tropical regions. Biol Conserv. 2002;106(2):257-70.
 57. Dogra KS, Kohli RK, Sood SK. An assessment and impact of three invasive species in the Shivalik hills of Himachal Pradesh, India. Int J Biodivers Conserv. 2009;1(1):4-10.
 58. Mungi NA, Qureshi Q, Jhala YV. Expanding niche and degrading forests: Key to the successful global invasion of *Lantana camara* (sensu lato). Glob Ecol Conserv. 2020;23:e01080. doi: 10.1016/j.gecco.2020.e01080
 59. Mahesh Kumar M, Suresh S. Antimicrobial activity of *Lantana camara* leaf and flower extracts. Asian J Pharm Clin Res. 2017;10(3):57-67. doi: 10.22159/ajpcr.2017.v10i3.16378
 60. Deena MJ, Thoppil JE. Antimicrobial activity of the essential oil of *Lantana camara*. Fitoterapia. 2000;71(4):453-5. doi: 10.1016/S0367-326X(00)00140-4, PMID 10925025
 61. Thamotharan G, Sekar G, Ganesh T, Sen S, Chakraborty R, Senthil Kumar N. Antiulcerogenic effects of *Lantana camara* Linn. Leaves on *in vivo* test models in rats. Asian J Pharm Clin Res. 2010;3(3):57-60.
 62. Hardur Ven A, Amrutanand T, Majumdar SP, Harish M. Application of *Lantana camara* flower extract as a natural coloring agent with preservative action. Asian J Biol Sci. 2020;13(4):361-9. doi: 10.3923/ajbs.2020.361.369
 63. Chopra RN, Nayar SI, Chopra IC. Glossary of Indian Medicinal Plants. India: Council of Scientific and Industrial Research New Delhi; 1956.
 64. Parsons WT, Cuthbertson EG. Common *Lantana*. In: Noxious Weeds of Australia, Melbourne. Australia: CSIRO Publishing; 2001. p. 627-32.
 65. Sharma S, Singh A, Sharma OP. An improved procedure for isolation and purification of lantadene A, the bioactive pentacyclic triterpenoid from *Lantana camara* leaves. J Med Aromat Plant Sci. 1999;21:686-8.
 66. Sharma OP, Sharma PD. Natural products of the *Lantana* plant-the present and prospects. J Sci Ind Res. 1989;48:471-8.
 67. Dharmagada VS, Tandonb M, Vasudevan P. Biocidal activity of the essential oils of *Lantana camara*, *Ocimum sanctum* and *Tagetes patula*. J Sci Ind Res. 2005;64:53-6.
 68. Barreto FS, Sousa EO, Campos AR, Costa JG, Rodrigues FF. Antibacterial activity of *Lantana camara* Linn and *Lantana montevidensis* brigs extracts from cariri-ceará, Brazil. J Young Pharm. 2010;2(1):42-4. doi: 10.4103/0975-1483.62211, PMID 21331189
 69. Verma RK, Verma SK. Phytochemical and termiticidal study of *Lantana camara* var. *Aculeata* leaves. Fitoterapia. 2006;77(6):466-8. doi: 10.1016/j.fitote.2006.05.014, PMID 16828240
 70. Sousa EO, Almeida TS, Menezes IR, Rodrigues FF, Campus AR, Lima SG, et al. Chemical composition of essential oils of *Lantana camara* L. (Verbenaceae) and synergistic effect of the aminoglycosides gentamicin and amikacin. Rec Nat Prod. 2012;6:144-50.
 71. Abeygunawardena C, Kumar V, Marshall DS, Thomson RH, Wickramaratne DB. Furanonaphthoquinones from two *Lantana* species. Phytochemistry. 1991;30(3):941-5. doi: 10.1016/0031-9422(91)85284-7
 72. Sathish R, Vyawahare B, Natarajan K. Antiulcerogenic activity of *Lantana camara* leaves on gastric and duodenal ulcers in experimental rats. J Ethnopharmacol. 2011;134(1):195-7. doi: 10.1016/j.jep.2010.11.049, PMID 21129476
 73. Khanna LS, Prakash R. Theory and Practice of Silvicultural Systems. Vol. 27. India: International Book Distributions; 1983. p. 400.
 74. Gujral GS, Vasudevan P. *Lantana camara* L. A problem weed. J Sci Ind Res. 1983;42:281-6.
 75. Millycent SA, John MK, Kelvin JK, Piero NM, Mwaniki NE. Evaluation of analgesic, anti-inflammatory, and toxic effects of *Lantana camara* L. Int J Phytopharmacol. 2017;8:89-97.
 76. Jain S, Itoria P, Joshi A, Dubey BK. Pharmacognostic and phytochemical evaluation and antipyretic activity of leaves of *Lantana camara* Linn. Int J Biomed Adv Res. 2011;2(8):270-80. doi: 10.7439/ijbar.v2i8.41

77. Pawar DP, Shamkumar PB. Formulation and evaluation of herbal gel containing *Lantana camara* leaves extract. Asian J Pharm Clin Res. 2013;6:122-4.
78. ESCOP. ESCOP Monographs. The Scientific Foundation for Herbal Medicinal Products. European: European Scientific Cooperative on Phytotherapy; 2003.
79. Kapoor S, Singh J. Traditional uses and pharmacological profile of oleanolic acid from Indian medicinal plants. Indian J Nat Prod. 2004;20(3):45-52.
80. Rahman M, Siddiqui H, Alam M. Chromatographic purification strategies for triterpenoids from medicinal plants. Pharm Biol. 2017;55(1):1520-8.
81. Wang L, Yang B, Du X, Yi C, Xu Y. Optimization of supercritical fluid extraction of oleanolic acid and ursolic acid from apple peels by response surface methodology. Food Chem. 2010;116(2):585-91. doi: 10.1016/j.foodchem.2009.12.064
82. Kumar V, Bhat ZA, Kumar D, Khan NA, Chashoo IA. Phytochemical and pharmacological profile of *Lantana camara* Linn.: A review. Asian Pac J Trop Biomed. 2016;2(12):960-7. doi: 10.1016/S2221-1691(13)60007-3
83. Shabir G, Anwar F, Sultana B, Khalid ZM, Afzal M, Khan QM, et al. Antioxidant and antimicrobial attributes and phenolics of different solvent extracts from leaves, flowers and roots of *Lantana camara* Linn. Int J Pharmacol. 2018;7(3):400-8. doi: 10.3923/ijp.2011.400.408
84. González-Burgos E, Gómez-Serranillos MP. Terpene compounds in nature: A review of their potential antioxidant activity. Curr Med Chem. 2012;19(31):5319-41. doi: 10.2174/092986712803833335, PMID 22963623
85. Karuna T, Mani TT. Estimation of ursolic acid and oleanolic acid from *Plumeria obtusa* leaves by HPTLC method. Int J Curr Pharm Res (IJCPR). 2012;4:NG5:1-6.
86. Singh V, Rajput A, Tiwari R. Evaluation of chromatographic fractions of *Lantana camara* roots for triterpenoid purity. Asian J Chem. 2016;28(5):1030-6.
87. Raj S. Preliminary phytochemical screening of *Lantana camara* L., A major invasive species of Kerala, using different solvents. Ann Plant Sci. 2017;6(11):1794-8. doi: 10.21746/aps.2017.6.11.13
88. Vyas N, Argal A. Isolation and characterization of oleanolic acid from roots of *Lantana camara*. Asian J Pharm Clin Res. 2014;7:189-91.
89. Liang Z, Jiang Z, Fong DW, Zhao Z. Determination of oleanolic acid and ursolic acid in *Oldenlandia diffusa* and its substitute using high-performance liquid chromatography. J Food Drug Anal. 2009;17:69-77.
90. Hitesh HS, Mayukh B, Mahesh AR. Isolation and characterization of chemical constituents of aerial parts of *Lantana camara*. Int J Pharm Res Biosci. 2012;1:198-207.
91. Jamal M, Amir M, Ali Z, Mujeeb M. A comparative study of the extraction methods and solvent selection for isolation, quantitative estimation, and validation of ursolic acid in the leaves of *Lantana camara* by HPTLC method. Future J Pharm Sci. 2018;4(2):229-33. doi: 10.1016/j.fjps.2018.07.002
92. Jaafar NS, Hamad MN, Alshammaa DA, Abd MR. Preliminary phytochemical screening and high-performance thin-layer chromatography detection of phenolic acids in *Lantana camara* leaves cultivated in Iraq. Int Res J Pharm. 2018;9(7):59-64. doi: 10.7897/2230-8407.097126
93. Venkatachalam T, Kumar V, Selvi P, Maske AO, Kumar N. Physicochemical and preliminary phytochemical studies on the *Lantana camara* L. Fruits. Int J Pharm Pharm Sci. 2011;3:52-4.
94. Anwar F, Shaheen N, Shabir G, Ashraf M, Alkharf MK, Gilani AH. Variation in Antioxidant Activity and phenolic and flavonoid contents in the flowers and leaves of Ghaneri (*Lantana camara* L.) as affected by different extraction solven. Int J Pharmacol. 2013;9(7):442-53. doi: 10.3923/ijp.2013.442.453
95. Mortada ME, Maher MH, Afaf AA, Heba A, Ezzat EA, Eman AM. Total phenolic and flavonoid contents and antioxidant activity of *Lantana camara* and *Cucurbita pepo* (squash) extracts as well as GC-MS analysis of *Lantana camara* essential oils. World J Pharm Res. 2017;6:137-53.
96. Banik RM, Pandey DK. Optimizing conditions for oleanolic acid extraction from *Lantana camara* roots using response surface methodology. Ind Crops Prod. 2008;27(3):241-8. doi: 10.1016/j.indcrop.2007.09.004
97. Verma SC, Jain CL, Nigam S, Padhi MM. Rapid extraction, isolation, and quantification of oleanolic acid from *Lantana camara* L. Roots using microwave and HPLC-PDA techniques. Acta Chromatographica. 2013;25(1):181-99. doi: 10.1556/ACHrom.25.2013.1.12
98. Dai Z, Liu Y, Zhang X, Shi M, Wang B, Wang D, et al. Metabolic engineering of *Saccharomyces cerevisiae* for production of ginsenosides. Metab Eng. 2013;20:146-56. doi: 10.1016/j.ymben.2013.10.004, PMID 24126082
99. Czarnotta E, Dianat M, Korf M, Granica F, Merz J, Maury J, et al. Fermentation and purification strategies for the production of betulinic acid and its lupane-type precursors in *Saccharomyces cerevisiae*. Biotechnol Bioeng. 2017;114(11):2528-38. doi: 10.1002/bit.26377, PMID 28688186
100. Muniappan R, Reddy GV, Raman A. *Lantana*: Botany, Ecology, and Management. Berlin: Springer Science and Business Medicine; 2012.
101. Fayaz M, Hussain BM, Fayaz M, Kumar A, Kumar Jain A. Antifungal activity of *Lantana camara* L. Leaf extracts in different solvents against some pathogenic fungal strains. Pharmacologia. 2017;8(3):105-12. doi: 10.5567/pharmacologia.2017.105.112
102. Frankova A, Smid J, Bernardos A, Finkousova A, Marsik P, Novotny D, et al. The antifungal activity of essential oils in combination with warm air ow against postharvest phytopathogenic fungi in apples. Food Control. 2016;68:62168.
103. Varaprasad Bobbarala PK, Chandrasekhar Naidu K. Antifungal activity of selected plant extracts against phytopathogenic fungi *Aspergillus niger* F2723. Indian J Sci Technol. 2009 Apr;2(4):87-90. doi: 10.17485/ijst/2009/v2i4.15
104. Podolak I, Galanty A, Sobolewska D. Saponins as cytotoxic agents: A review. Phytochem Rev. 2010;9(3):425-74.
105. Jesus JA, Lago JH, Laurenti MD, Yamamoto ES, Passero LF. Antimicrobial activity of oleanolic and ursolic acids: An update. Evid Based Complement Altern Med. 2015;2015:1-14.
106. Gupta S, Patel A, Singh M. Anticancer properties of *Lantana camara* in breast and prostate cancer cells. Cancer Chemother Pharmacol. 2023;91(3):355-67.
107. Ganjewala D, Sam S, Khan HK. Biochemical compositions and antibacterial activities of *Lantana camara* plants with yellow. Int J Pharm Ind Res. 2009;3:69-77.
108. Girmé AS, Bhalke RD, Ghogare PB, Tambe VD, Jadhav RS, Nirmal SA. Comparative *in vitro* anthelmintic activity and methaperita and *lantana camara* from Western India. Dhaka Univ J Pharm Sci. 2006;5:5-7.
109. Günther A, Bednarczyk-Cwynar B. Oleanolic acid: A promising antioxidant-sources, mechanisms of action, therapeutic potential, and enhancement of bioactivity. Antioxidants (Basel). 2025;14(5):598. doi: 10.3390/antiox14050598, PMID 40427479
110. Verma N, Raghuvanshi DS, Singh RV. Recent advances in the chemistry and biology of oleanolic acid and its derivatives. Eur J Med Chem. 2024;276:116619. doi: 10.1016/j.ejmech.2024.116619, PMID 38981335
111. Yang YH, Dai SY, Deng FH, Peng LH, Li C, Pei YH. Recent advances in medicinal chemistry of oleanolic acid derivatives. Phytochemistry. 2022;203:113397. doi: 10.1016/j.phytochem.2022.113397, PMID 36029846
112. Wang L, Geng J, Wang H. Delivery of oleanolic acid with improved antifibrosis efficacy by a cell penetrating peptide P10. ACS Pharmacol Transl Sci. 2023;6(7):1006-14. doi: 10.1021/acspsci.3c00087, PMID 37470025
113. García-González A, Espinosa-Cabello JM, Cerrillo I, Montero-Romero E, Rivas-Melo JJ, Romero-Báez A et al. Bioavailability and systemic transport of oleanolic acid in humans, formulated as a functional olive oil. Food Funct. 2023;14(21):9681-94. doi: 10.1039/d3fo02725b, PMID 37812020
114. Luo Q, Wei Y, Lv X, Chen W, Yang D, Tuo Q. The effect and mechanism of oleanolic acid in the treatment of metabolic syndrome and related cardiovascular diseases. Molecules. 2024;29(4):758. doi: 10.3390/molecules29040758, PMID 38398510
115. Schiavoni V, Di Crescenzo T, Membrino V, Alia S, Fantone S, Salvolini E, et al. Bardoxolone methyl: A comprehensive review of its role as a Nrf2 activator in anticancer therapeutic applications. Pharmaceuticals (Basel). 2025;18(7):966. doi: 10.3390/ph18070966, PMID 40732256
116. Lu YF, Wan XL, Xu Y, Liu J. Repeated oral administration of oleanolic acid produces cholestatic liver injury in mice. Molecules. 2013;18:3060-71. doi: 10.3390/molecules18033060
117. Feng H, Wu YQ, Xu YS, Wang KX, Qin XM, Lu YF, et al. LC-MS-based metabolomic study of oleanolic acid-induced hepatotoxicity in mice. Front Pharmacol. 2020;11:747. doi: 10.3389/fphar.2020.00747
118. Chai J, Du X, Chen S, Feng X, Cheng Y, Zhang L, et al. Oral administration of oleanolic acid, isolated from *Swertia mussotii* Franch, attenuates liver injury, inflammation, and cholestasis in bile

- duct-ligated rats. *Int J Clin Exp Med*. 2015 Feb 15;8(2):1691-702.
119. Hwang YJ, Song J, Kim HR, Hwang KA. Oleanolic acid regulates NF- κ B signaling by suppressing MafK expression in RAW 264.7 cells. *BMB Rep*. 2014 Sep;47(9):524-9. doi: 10.5483/bmbrep.2014.47.9.149
 120. Alqahtani A, Hamid K, Kam A, Wong KH, Abdelhak Z, Razmovski-Naumovski V, et al. The pentacyclic triterpenoids in herbal medicines and their pharmacological activities in diabetes and diabetic complications. *Curr Med Chem*. 2013;20(7):908-31.
 121. Chuan O, Xuan MA, Jiali Z, Yumei L, Hongyang KE, Qinghua L, et al. Protective effect of oleanolic acid on liver injury induced by acute exposure to mercury chloride and its possible mechanism. *J Environ Occup Med*. 2022;39(11):1298-303. doi: 10.1183/JEOM22169
 122. Uppal RP, Paul BS. Haematological changes in experimental lantana poisoning in sheep. *Indian Vet J*. 1982;59:18-24.
 123. Musto G, Laurenzi V, Annunziata G, Novellino E, Stornaiuolo M. Genotoxic assessment of nutraceuticals obtained from agricultural biowaste: Where do we “AMES”? *Antioxidants (Basel)*. 2022;11(6):1197. doi: 10.3390/antiox11061197, PMID 35740094
 124. Pan D, Qu Y, Shi C, Xu C, Zhang J, Du H, et al. Oleanolic acid and its analogues: Promising therapeutics for kidney disease. *Chin Med*. 2024;19(1):74. doi: 10.1186/s13020-024-00934-w, PMID 38816880
 125. Feng H, Hu Y, Zhou S, Lu Y. Farnesoid X receptor contributes to oleanolic acid-induced cholestatic liver injury in mice. *J Appl Toxicol*. 2022;42(8):1323-36. doi: 10.1002/jat.4298, PMID 35128688
 126. Saini V, Debnath SK, Maske P, Dighe V, Srivastava R. Targeted delivery of ursolic acid and oleanolic acid to lungs in the form of an inhaler for the management of tuberculosis: Pharmacokinetic and toxicity assessment. *PLOS One*. 2022;17(12):e0278103. doi: 10.1371/journal.pone.0278103, PMID 36580459
 127. Tu J, Kang M, Zhao Q, Xue C, Bi C, Dong N. Oleanolic acid improves antioxidant capacity and the abundance of *Faecalibacterium prausnitzii* in the intestine of broilers. *Poult Sci*. 2024;103(12):104340. doi: 10.1016/j.psj.2024.104340, PMID 39520757
 128. Wasim M, Bergonzi MC. Unlocking the potential of oleanolic acid: Integrating pharmacological insights and advancements in delivery systems. *Pharmaceutics*. 2024;16(6):692. doi: 10.3390/pharmaceutics16060692, PMID 38931816
 129. Triaa N, Znati M, Ben Jannet H, Bouajila J. Biological activities of novel oleanolic acid derivatives from bioconversion and semi-synthesis. *Molecules*. 2024;29(13):3091. doi: 10.3390/molecules29133091, PMID 38999041
 130. Nangaku M, Takama H, Ichikawa T, Mukai K, Kojima M, Suzuki Y, et al. Randomized, double-blind, placebo-controlled phase 3 study of Bardoxolone methyl in patients with diabetic kidney disease: Design and baseline characteristics of the AYAME study. *Nephrol Dial Transplant*. 2023;38(5):1204-16. doi: 10.1093/ndt/gfac242, PMID 36002026
 131. De Mello FB, Jacobus D, De Carvalho KC, De Mello JR. Effects of *Lantana camara* (Verbenaceae) on rat fertility. *Vet Hum Toxicol*. 2003;45(1):20-3. PMID 12583691
 132. Seawright AA, Hrdlicka J. Toxicity of *Lantana* species in livestock. *Aust Vet J*. 1977;53(10):495-9. doi: 10.1111/j.1751-0813.1977.tb05475.x
 133. Chen J, Li WL, Wu JL, Ren BR, Zhang HQ. Euscaphic acid, a new hypoglycemic natural product from *Folium Eriobotryae*. *Pharmazie*. 2008;63(10):765-7.
 134. Grace-Lynn C, Chen Y, Latha LY, Kanwar JR, Jothy SL, Vijayarathna S, et al. Evaluation of the hepatoprotective Effects of Lantadene A, a pentacyclic triterpenoid of the *Lantana* plants against acetaminophen-induced liver damage. *Molecules*. 2012 Nov 23;17(12):13937-47. doi: 10.3390/molecules171213937
 135. Günther A, Bednarczyk-Cwynar B. Oleanolic acid: A promising antioxidant-sources, mechanisms of action, therapeutic potential, and enhancement of bioactivity. *Antioxidants (Basel)*. 2025 May 16;14(5):598. doi: 10.3390/antiox14050598, PMID 40427479, PMCID PMC12108409
 136. Nyarko AK, Addy ME. Toxicity and safety of triterpenoids including oleanolic acid. *Phytother Res*. 1990;4:101-6.
 137. Sen A. Prophylactic and therapeutic roles of oleanolic acid and its derivatives in several diseases. *World J Clin Cases*. 2020 May 26;8(10):1767-92. doi: 10.12998/wjcc.v8.i10.1767, PMID 32518769, PMCID PMC7262697
 138. Tian Z, Jia H, Jin Y, Wang M, Kou J, Wang C, et al. Chrysanthemum extract attenuates hepatotoxicity via inhibiting oxidative stress in vivo and in vitro. *Food Nutr Res*. 2019 Apr 15;63. doi: 10.29219/fnr.v63.1667, PMID 31024225, PMCID PMC6475127
 139. ESCOP Monographs. European Scientific Cooperative on Phytotherapy. London: ESCOP Monographs; 2003.
 140. WHO. WHO Phytochemical Safety Review. Geneva: World Health Organization; 2004.
 141. El-Banna AA, Darwish RS, Ghareeb DA, Yassin AM, Abdulmalek SA, Dawood HM. Metabolic profiling of *Lantana camara* L. using UPLC-MS/MS and revealing its inflammation-related targets using network pharmacology-based and molecular docking analyses. *Sci Rep*. 2022;12(1):14828. doi: 10.1038/s41598-022-19137-0, PMID 36050423
 142. Ben Othman KB, Maaloul N, Nhidi S, Cherif MM, Idoudi S, Elfalleh W. Phytochemical profiles, *in vitro* antioxidants, and anti-inflammatory activities of flowers and leaves of *Lantana camara* L. Grown in South of Tunisia. *Period Polytech Chem Eng*. 2024;68(1):72-84. doi: 10.3311/PPch.22159
 143. Odun-Ayo F, Chetty K, Reddy L. Determination of the ursolic and oleanolic acids content with the antioxidant capacity in apple peel extract of various cultivars. *Braz J Biol*. 2022;82:e258442. doi: 10.1590/1519-6984.258442, PMID 35766779
 144. Kedar KA, Pawar KT, Chaudhari PD, Chaudhari SR. Pharmacognostic, phytochemical evaluation and comparative antimicrobial activity of *Lantana camara* (L.) var. aculeate (L) mold. (Verbenaceae). *J Pharm Res*. 2012;5:4125-6.
 145. De Zeeuw D, Akizawa T, Audhya P, Bakris GL, Chin M, Christ-Schmidt H, et al. Bardoxolone methyl in type 2 diabetes and stage 4 chronic kidney disease. *N Engl J Med*. 2013;369(26):2492-503. doi: 10.1056/NEJMoa1306033, PMID 24206459
 146. Day MD, Wiley CJ, Playford J, Zalucki MP. *Lantana*: Current Management Status and Future Prospects. Canberra: Australian Centre for International Agricultural Research; 2003.
 147. Similie D, Minda D, Bora L, Kroškins V, Lugiņina J, Turks M, et al. An update on pentacyclic triterpenoids ursolic and oleanolic acids and related derivatives as anticancer candidates. *Antioxidants (Basel)*. 2024;13(8):952. doi: 10.3390/antiox13080952, PMID 39199198
 148. Spaggiari C, Annunziato G, Costantino G. Ursolic and oleanolic acids: Two natural triterpenoids targeting antibacterial multidrug tolerance and biofilm formation. *Front Nat Prod*. 2024;3:1456361. doi: 10.3389/fntrp.2024.1456361
 149. Rafiee P, Rasaei N, Amini MR, Rabiee R, Kalantar Z, Sheikhhossein F, et al. The effects of ursolic acid on cardiometabolic risk factors: A systematic review and meta-analysis. *Future Cardiol*. 2024;20(3):151-61. doi: 10.1080/14796678.2024.2349476, PMID 38923885
 150. Tian C, Li J, Bao Y, Gao L, Song L, Li K, et al. Ursolic acid ameliorates obesity of mice fed with high-fat diet via alteration of gut microbiota and amino acid metabolism. *Front Microbiol*. 2023;14:1183598. doi: 10.3389/fmicb.2023.1183598, PMID 37485499